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INVESTIGATIONS OF INTER- AND INTRAMOLECULAR C-O BOND FORMING REACTIONS OF PEROXIDE ELECTROPHILES

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INVESTIGATIONS OF INTER- AND INTRAMOLECULAR C-O BOND FORMING REACTIONS OF PEROXIDE ELECTROPHILES

by

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INVESTIGATIONS OF INTER- AND INTRAMOLECULAR C-O BOND FORMING REACTIONS OF PEROXIDE ELECTROPHILES

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A common reaction to yield ethers relies on an alkoxide nucleophile and a carbon electrophile (Williamson ether formation). Ethers can also be formed by reactions with carbon nucleophiles and oxygen electrophiles by way of the peroxide functional group. We screened a number of carbon nucleophiles suitable for attack on dialkyl peroxides to form new C-O bonds. Also a novel approach using a peroxyketal electrophile is shown to increase the efficiency of this intermolecular reaction. This method of C-O bond formation can also be implemented intramolecularly, not seen before in the literature, to yield cyclic ethers. This approach requires the generation of an organolithium, *via* lithium/heteroatom exchange, in the presence of a peroxide. The intramolecular C-O bond formation is shown here to yield 5 and 6-membered ethers as well as oxetenes.

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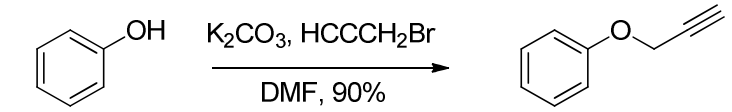
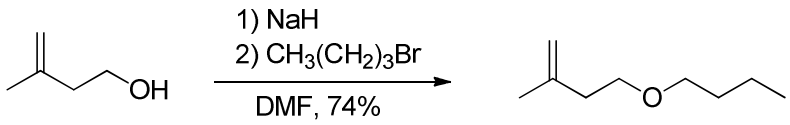
Introduction

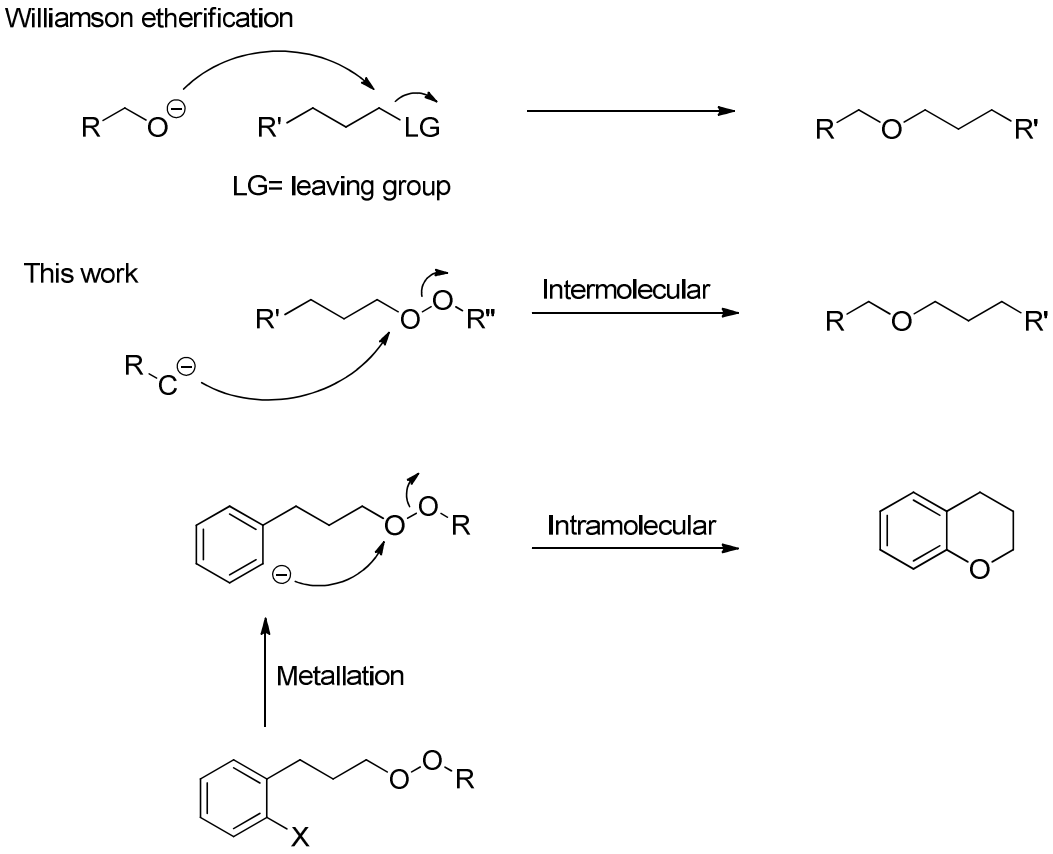
The Williamson ether synthesis is one of the most well-known reactions in chemistry for making ethers. [1] In a typical procedure an alcohol is deprotonated with a base such as NaH or phenol is deprotonated with potassium carbonate, and the resulting alkoxide or phenoxide is reacted a primary alkyl halide (or a functionally similar species such as an alkyl sulfonate) in a polar aprotic solvent to yield ethers. Typical examples are shown below. [2,3]





The Williamson etherification is based upon on the nucleophilicity of the oxygen of an alcohol functionality and the elctrophilicity of a corresponding carbon species. In the work presented here we will demonstrate a reversal in the polarity of the carbon and oxygen reactants involved in the C-O bond forming reaction. In this thesis, we will demonstrate new approaches to ethers based upon umpoled reactivity, the attack of carbanion nucleophiles on the O-O bond of a peroxide. Also included will be the synthesis of cyclic ethers, which involves generation of the carbon nucleophile in the presence of the peroxide electrophile (intramolecular). **Scheme 1** illustrates the role reversal of oxygen and carbon and an example of intramolecular vs. intermolecular reactions.

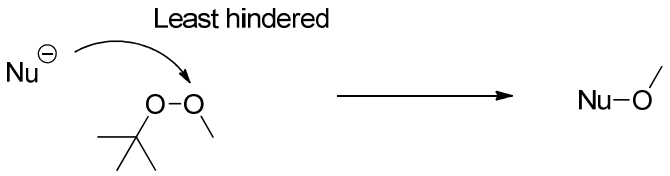
Scheme 1



Previous work in the literature shows carbon nucleophiles reacting with peroxides to form ethers. The earliest reports of this reaction are from Gilman and Adams who showed that phenylmagnesium bromide reacts with diethyl peroxide to give a 34% yield of ethyl phenyl ether. [(4)] Organo-lithium, as well as Grignard reagents, serve as carbon nucleophiles and will attack peroxides to give ethers. The table below shows work form Baramki and coworkers.[(5)] It is important to note, that due to steric hindrance of the tert-butyl group, only the corresponding methyl ether products were observed (see **Scheme 2**). Reactions with di-*tert*butyl peroxide and phenyl magnesium bromide yielded no ether product. The Grignard reagents may be more susceptible to steric influences because of

their lower nucleophilicity and the need for Lewis acid activation of the peroxide. The more nucleophilic organo-lithium carbon nucleophiles give better yields of the desired ether products.

Scheme 2



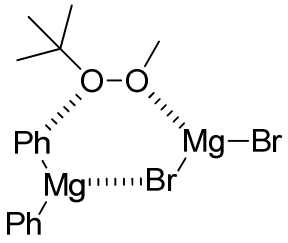
Peroxide	Reaction Temp. (°C)	Yield (%) from PhLi	Yield (%) from PhMgBr
Dimethyl	15-20	80	77
Methyl t-butyl	15-20	63	20
methyl t-butyl	35	72	38
Diethyl	15-20	38	30
Di-t-butyl	0-5	3.3	-
Di-t-butyl	15-20	19	-
Di-t-butyl	35	39	0
Di-t-butyl	80	38	0

The generally accepted mechanism for the ether formation shown above is an S_N2 displacement in which formation of the new C-O bond corresponds with the breaking of the O-O bond of the peroxide. Other mechanisms have been proposed, involving alkoxy radical intermediates, to explain a variety of side products. [5-7] **Scheme 3a** shows an alternate mechanism for a reaction of a Grignard reagent with a dialkyl peroxide. **Scheme 3b** overviews a suggested radical mechanism for organo-lithium reagents that accounts for a number of observed side products. The radical mechanism involves generation of an alkoxy radical in a solvent cage along with the carbon radical. Coupling between these

two radicals in the solvent cage generates a new C-O bond, whereas diffusion out of this cage allows for formation of many of the observed side products.

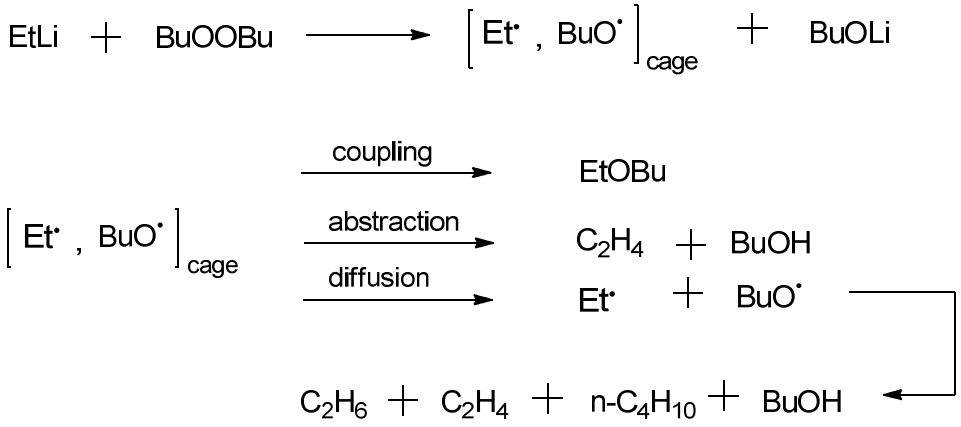
Scheme 3a

Baramki and coworkers



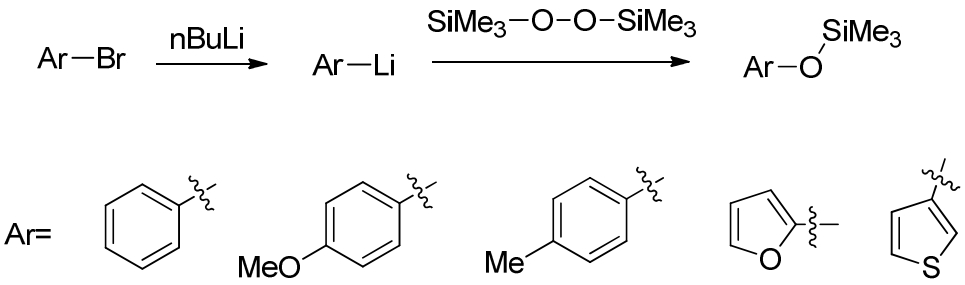
Scheme 3b

Kochi and coworkers



Taddei and coworkers employed the reaction of organolithium reagents and silyl peroxides to generate silyl enol ethers. **Scheme 4** begins with formation of an organolithium by lithium/bromide exchange. The resulting organolithium nucleophile is then reacted with a peroxide electrophile, in this case, a di-silyl peroxide - $(Me_3Si)_2O_2$. [8, 9]

Scheme 4

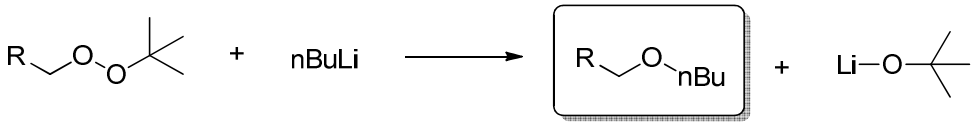


Part I: Intermolecular C-O Bond Formation

Introduction

This chapter will discuss intermolecular C-O bond forming reactions of carbon nucleophiles with peroxides; an example is shown in **Scheme 5**. Work in this chapter will focus on a screening of carbon nucleophiles suitable for this type of C-O bond formation. Also examined will be a peroxy acetal not seen before in the literature that increases the efficiency of the C-O bond formation. A significant increase in yield and reactivity is observed when a chelating peroxyketal is incorporated into the molecule**. Scheme 5** below shows an example of intermolecular C-O bond formation using a carbon nucleophile and the peroxide electrophile. Notice the selectivity of attack at the least hindered oxygen of the peroxide.

Scheme 5



Results/Discussion

A model peroxide prepared from citronellol was employed in order to screen intermolecular C-O bond forming reactions. **Scheme 6** below outlines the short synthesis to the model substrate. The alcohol was converted to a good leaving group (methanesulfonate) by a conventional method. The resulting methanesulfonate was displaced by *tert*-butyl peroxycesium or the cesium salt of 2-hydroperoxy-2-methoxy propane, preformed by the mixing of *tert*-butyl hydroperoxide and $CsOH•H_2O$ to form **2** or **3**. [10] With the model substrate in hand, a screening of multiple carbon nucleophiles was performed.

Scheme 6

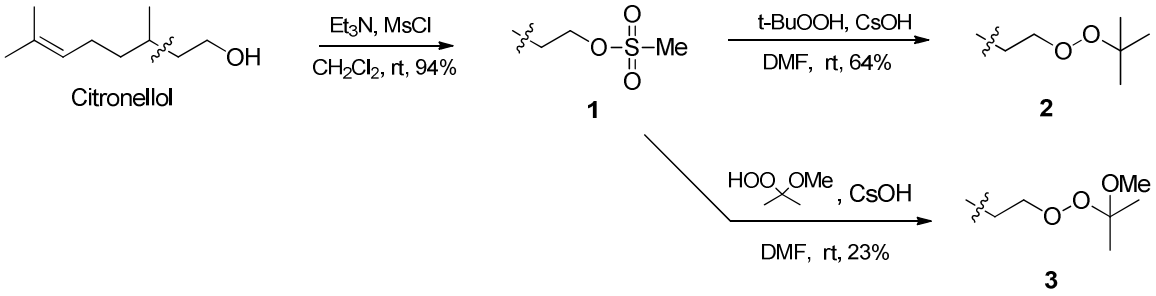
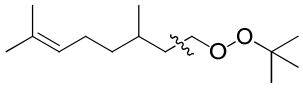
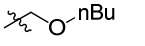
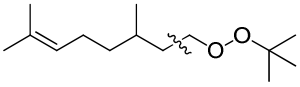
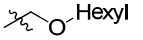
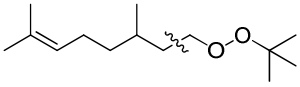
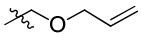
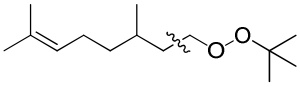
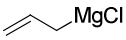
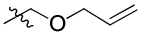
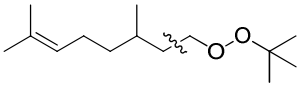
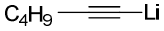
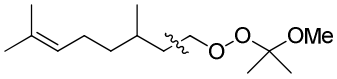
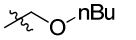


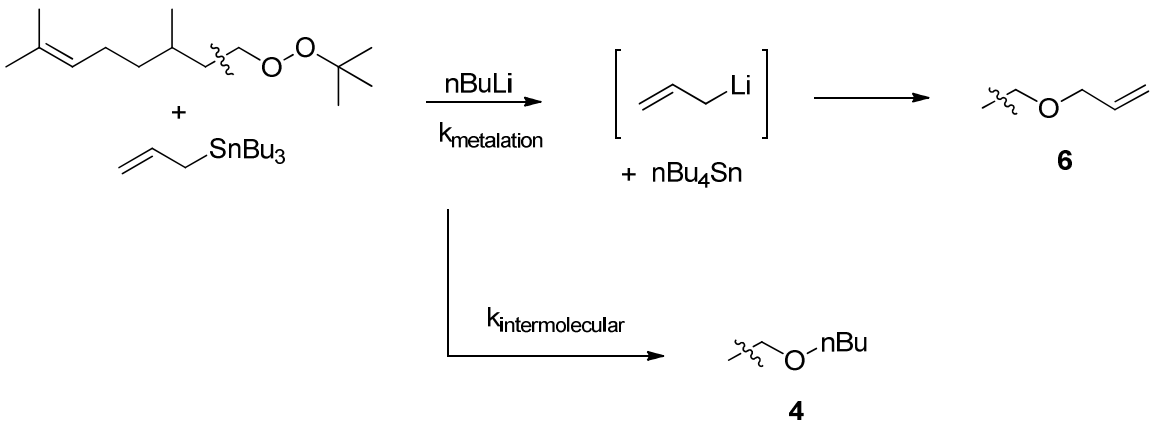
Table 1 below shows the results obtained from reacting several carbon nucleophiles with our model peroxide substrates. In accordance with previous literature, an organolithium nucleophile gave better yields than a Grignard reagent. A variety of additives were investigated for the ability to improve the yield of the intermolecular C-O bond formation ($CeCl_3$, $BF_3•OEt_2$, CuI, TMS-Cl, and CuCN). All failed to give improved yields. Entry number three is of particular interest. In this reaction, the model substrate

peroxide and allyl tributyltin were stirred together followed by the slow addition of nBuLi at -78^{o}C. The results require a tin-lithium exchange between allytributyl tin and nBuLi (metallation), generating an allyl-lithium, which then attacks the peroxide electrophile. Moreover, the outcome indicates a significantly higher rate for tin/lithium exchange ($k_{metallation}$) versus direct attack ($k_{intermolecular}$) of the nBuLi on the peroxide at -78 ^{o}C. This reaction has implications to the next chapter where we will discuss intramolecular reactions of organolithium reagents and peroxides.

Table 1

Entry	Substrate	RM	Rxn time (h)	Product		yield (%)
1		nBuLi	0.5		(**4**)	63
2		HexylMgBr	3		(**5**)	42
3			3		(**6**)	70
4			3		(**6**)	27
5[a]			48	Recov. SM		-
6		nBuLi	0.1		(**4**)	87

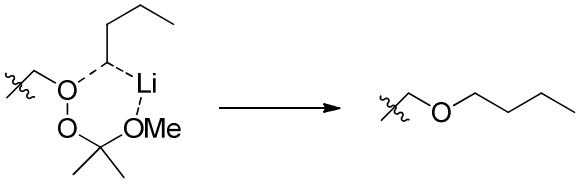
[a] Entry 5 at room temp.



Entry four in **Table 1** demonstrates that an alkynyl lithium was unsuccessful as a nucleophile; the peroxide was recovered after two days of stirring with organolithium. Reaction with our model peroxide and phenyllithium also failed to deliver a significant reaction; a small amount of phenylether was detected in the crude ^{1}H NMR spectrum. As may be expected, it appears that phenyl lithium falls between nBuLi and alkynyllithium in reactivity for attack on our model peroxide substrate.

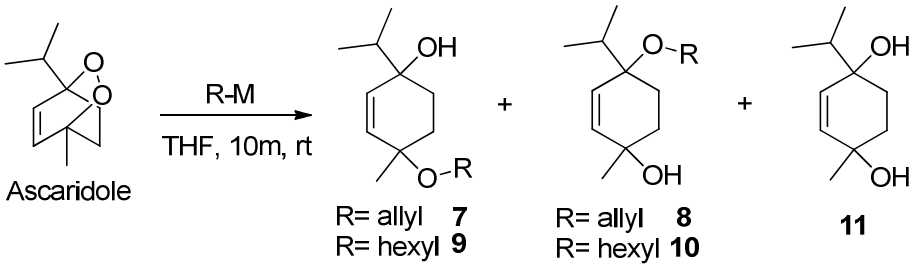
The final entry in **Table 1** is a slightly different peroxide. This peroxyketal substrate has an additional basic oxygen that may "direct" the organo-lithium nucleophile via a Lewis acid/Lewis base interaction shown in **Scheme 7.** The reaction of this substrate proceeds in a significantly increased yield compared with a simply dialkyl peroxide. The application of the chelating peroxyketal group has not been seen before in the literature. This directing affect serves to increase the efficiency of the reaction, both in terms of reaction rate and yield.

Scheme 7: Chelating group for C-O bond formation



To gain a better sense of the intermolecular C-O bond forming reactions, we turned to ascaridole, a substrate previously investigated in the literature.[11] Ascaridole is a convenient substrate, because the products of opening this cyclic peroxide will include both oxygens atoms. With this substrate we investigated the selectivity of which oxygen is attacked (**7** vs. **8**). We will also discuss the unexplained curious observation where a reduction of the peroxide yields large amounts of the diol product **9**. Allylated product **8** was not isolated.

Scheme 8



R-M	% yield (product)		
Allyl-MgCl	21 (**7**)	-	60 (**11**)
Hexyl-MgBr	24 (**9**)	10 (**10**)	48 (**11**)

Scheme 8 show the results of reactions of two Grignard reagents with ascaridole. The products show a slight preference for attack at the least hindered oxygen, but the major product is the diol. The high yield of diol is still somewhat of a mystery, given that

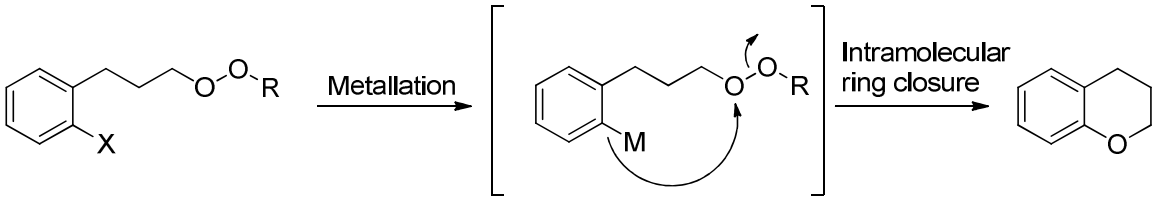
similar reactions were reported to furnish high yields of ether; there was no mention of the diol product.[11]

Part II: Intramolecular C-O bond formation

Introduction

Chapter II will focus on our efforts towards achieving the same C-O bond formation through reaction of carbon nucleophile and an oxygen electrophile. However, we will now focus on intramolecular reactions. **Scheme 9** depicts our goal, the generation of a carbanion nucleophile in the presence of a peroxide, which can subsequently undergo an intramolecular reaction to create a cyclic ether.

Scheme 9

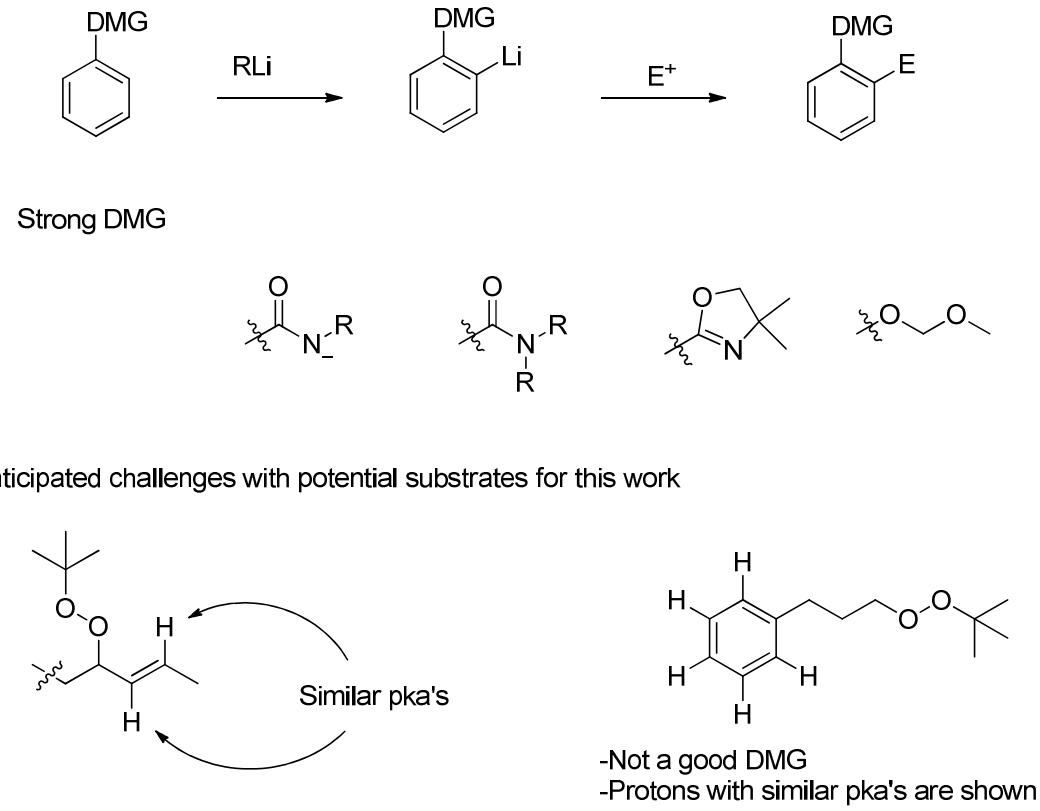


There are many ways of potentially generating this organo-lithium; in this section we will discuss deprotonation versus lithium/heteroatom exchange. Ultimately this will explain our preference for lithiation via lithium/heteroatom exchange.

The first process we will examine is deprotonation, the formation of an organometallic via removal of a proton by a base. A recent review outlines the utility of this type of metallation in organic synthesis. [12] For our systems we would be ultimately

interested in deprotonating an sp^2 carbon. Some draw backs to this approach include harsh reaction conditions and little control over protons with similar acidities. In order to get reasonable selectivity in the aryl systems, a good directing metallation group (DMG) would be required, which would limit our selection of substrates. Furthermore we were concerned about the stability of the peroxides under these conditions. **Scheme 10** below depicts potential problems with this approach.

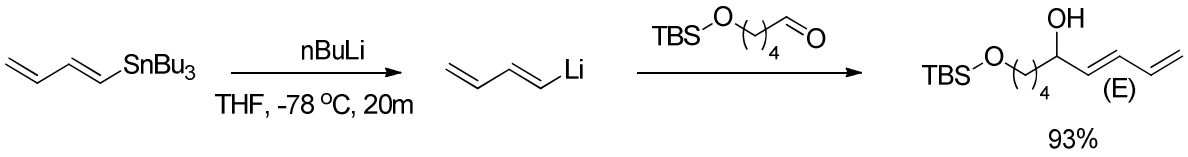
Scheme 10



Lithium/heteroatom exchange is appealing for two reasons. Depending on the heteroatom, the rate of lithiation will be very high, and equally important the stereochemistry of the heteroatom is retained after conversion to the organo-lithium. An

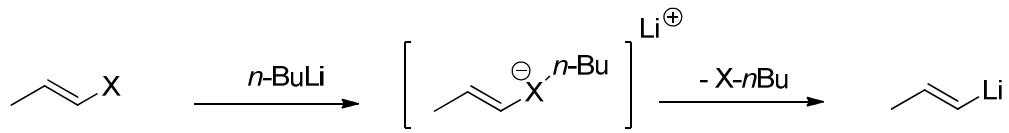
example from Nishiyama and co-works, shown in **Scheme 11**, shows the excellent yield and the fully retained (E) stereochemistry using lithium/tin exchange. [13]

Scheme 11



Lithium/heteroatom exchange proceeds through attack of the organolithium on the heteroatom to generate intermediates known as ate complexes. The ate complex can either release the original organolithium (regenerating starting material) or release a new organometallic. The reaction equilibrium is dominated by the formation of the most stable organolithium. This process occurs for a number of heteroatoms including, but not limited to, Sn, Te, Se, I, and Br. [14, 15] **Scheme 12** below depicts generation of the ate complex, and liberation of the new organolithium species.

Scheme 12

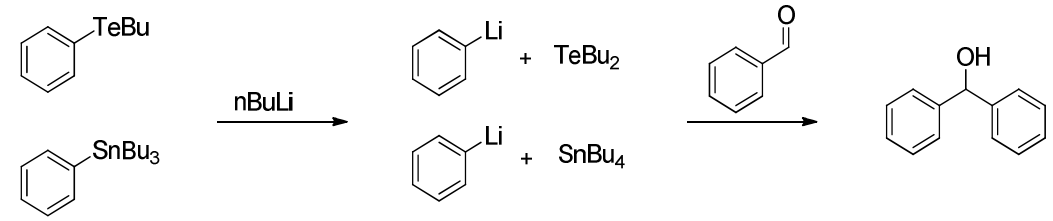


Kanda, Kambe, and coworkers performed competitive reactions to determine relative rates of lithium/heteroatom exchange for different heteroatoms. Their work is summarized in the **Table 2** below. The results show iodine having the highest rate

followed by the TeR, SnR_3, and finally SeR. [16] The importance of the rate of lithium/heteroatom exchange will be examined in more detail for our peroxide substrate.

Table 2: Relative rates of Lithium/Heteroatom exchange

Example:



ratio of $TeBu_2/SnBu_4$ used to determine relative rates

Competitive exchange reactions of PhM (M= SeBu, $SnBu_3$, $SnMe_3$, TeBu, I) and PhTeBu with BuLi at -70°C[a]

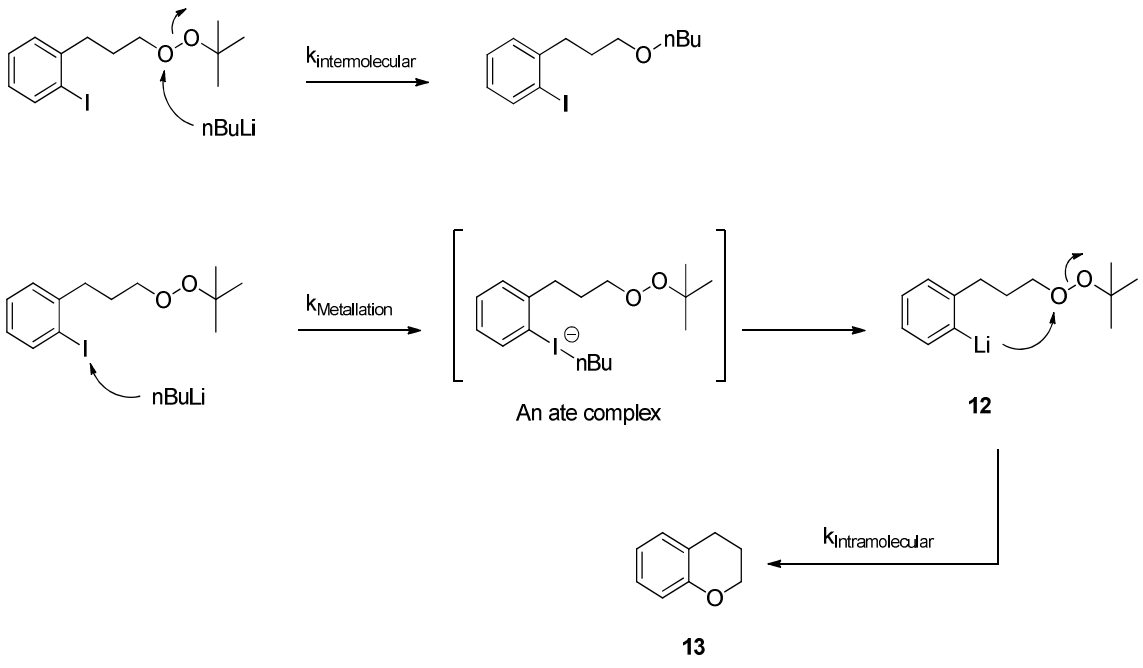
		GLC yields based on BuLi (%)				
Run	PhM: M	Bu_2Te	BuM	Ph_2CHOH	PhBuCHOH	ratio Bu_2Te/BuM
1	I	7	27	35	66	0.3
2	TeBu	13	13	28	74	1.0
3	*$SnBu_3$[b]	5	Trace	5	73	~300
4	*$SnBu_3$[c]	10	0.1	10	85	99
5	*$SnBu_3$	13	0.6	13	87	22
6	$SnBu_3$[d]	3	2	5	89	1.4
7	$SnMe_3$	9	8	18	80	1.1
8	SeBu	12	Trace	13	86	~300
9[e]	SeBu	7[f]	0.5[1]	8[1]	82[1]	15[g]

[a] Reaction conditions: PhTeBu (1 mmol), PhM (1 mmol), BuLi (0.2 mmol), THF (10ml), -70°, 15m, NH_4Cl_{aq}.
[b] Hexane (10ml) insted of THF.
[c] Et_2O (10ml) instead of THF.
[d] In the presence of HMPA (0.8 mmol).
[e] Competive reaction fo $PhSnBu_3$ and PhSeBu.
[f] Yield of Bu_4Sn.
[g] Bu_4Sn/Bu_2Se ratio.

Result/Discussion

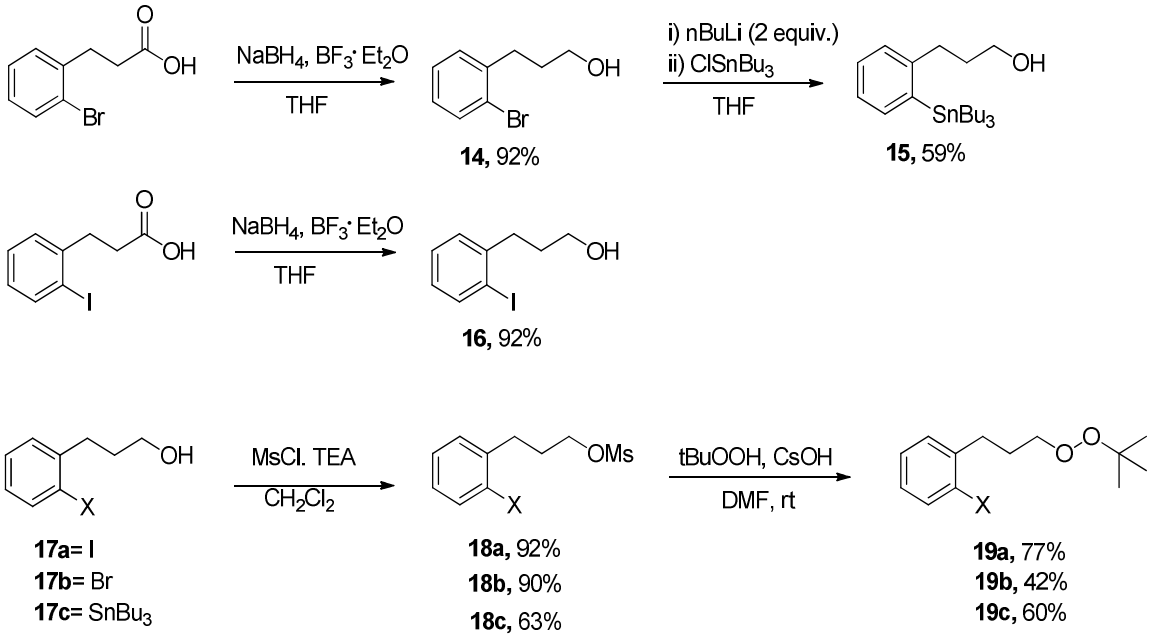
Our proposed intramolecular C-O bond foramtion is significantly more complicated due to the fact that the organo-lithium nucleophile must be generated in the presence of the peroxide moiety; (organolithium was chosen because of the superior results in the intermolecular screens). The organolithiums can be generated, for example, by lithium/heteroatom exchange with an aryl iodide and nBuLi yielding an aryl lithium **12**, an exchange driven by the stability of the resulting carbanion. However the same nBuLi could also attack the peroxide intermolecularly, as seen in the model work. Therefore the heteroatom/lithium exchange ($k_{metallation}$) must take place at a considerably faster rate than the competing intermolecular attack ($k_{intermolecular}$) of nBuLi on the peroxide. Once the organo-lithium **12** has been selectively generated *in situ*, the desired C-O bond forming reaction can take place to form the cyclic ether **13**.

Scheme 13: Mechanism for ring closing/competing reaction rates



We focused our initial attention on 6-*exo* cyclizations based upon Ar-I, Ar-Br, and Ar-$SnBu_3$ substrates, all of which are capable of undergoing similar lithium/heteroatom exchange. The synthesis of substrates is depicted in **Scheme 14** below.

Scheme 14: Synthetic routes to precursors for 6-*exo* cyclizations

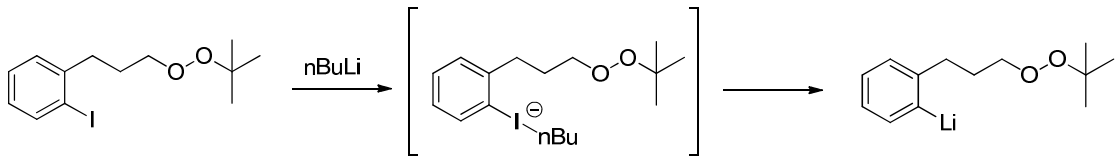


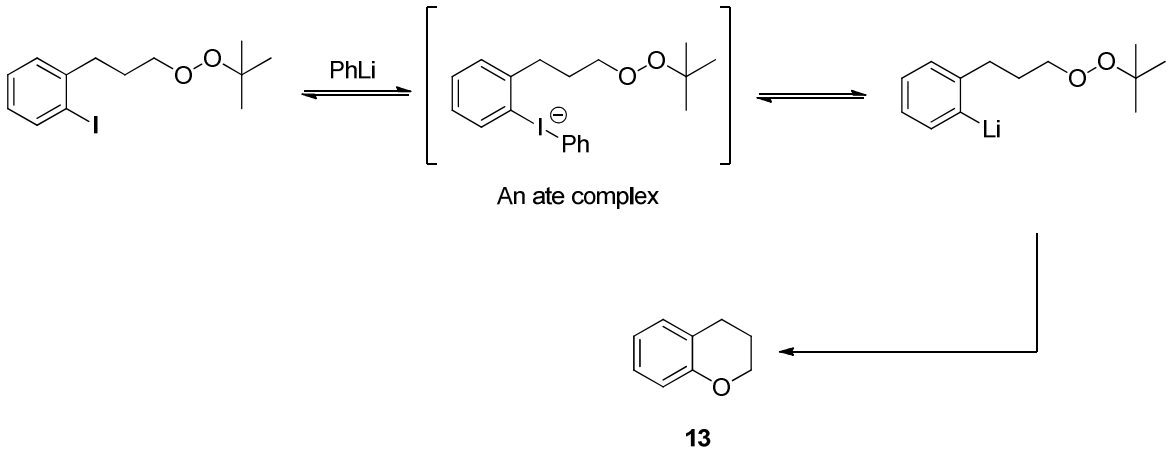
Reductions of commercially available haloarene acids were performed using the combination of $NaBH_4$ and BF_3•OEt_2. The active reducing agent generated in situ, BH_3, is able to achieve reduction of the carboxylic acids in high yield without dehalogenation of the iodo- or bromoarenes.[17] Stannane **15** is formed by lithiation of aryl-Br **14** followed by addition of electrophilic tin, $ClSnBu_3$, to give compound **15** in 59% yield. The iodophenyl-, bromophenyl-, and tributylstannyl phenyl propanols (**17a, 17b, 17c**) were each converted to the methanesulfonate uneventfully. The methanesulfonates were

then displaced by tBuOOH in the presence of $CsOH•H_2O$. Displacement was found to be higher yielding if the DMF solution of tBuOOH and CsOH was allowed to stir for 0.5 – 1 hour prior to addition of the methanesulfonates **18**, presumably allowing time for the preformation of the peroxycesium species from the poorly soluble cesium hydroxide.

The first step in the intramolecular C-O bond forming reaction is the formation of an ate complex upon addition of an organolithium. The process is illustrated for the aryl iodide (**Scheme 15**). The ate complex can decompose in the reverse direction to reform starting materials or in the forward direction to form the aryl lithium intermediate. When the organo-lithium reagent is nBuLi the forward reaction is favored largely ($K_{eq}>>1$) because of the fact that the aryl lithium is more stable than is the alkyl lithium. If a less basic organolithium (e.g. PhLi) is employed, the equilibrium between the starting material and the desired aryl lithium we be closer to 1. The aryl lithium can then perform the subsequent ring closure, effectively driving the reaction forward. The literature shows an iodoarene undergoing lithium/heteroatom exchange at the fastest rate followed by aryl-Br and finally aryl-$SnBu_3$.[18] In most literature reports both the aryl-I and aryl-Br undergo lithium/heteroatom exchange with nBuLi at a fast enough rate to give similar yields. [18-21]

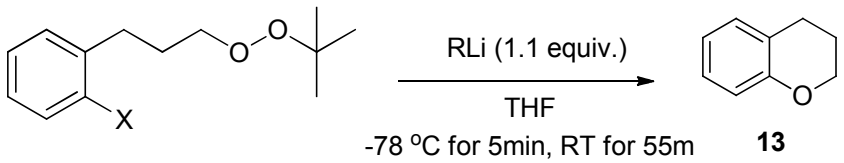
Scheme 15: Generation of organo-lithium *in situ*





The results of our experiments are summarized in **Table 3**. The substrates prepared as described in Scheme **14** were then reacted with nBuLi and phenyl lithium in THF. A GC equipped with a flame ionization detector (GC-FID) was used to determine yields due to difficulty purifying and isolated the volatile cyclic ether product **13**. Using pure sample of dihydrobenzopyran **13,** five standard solutions were prepared to calibrate responses on the GC-FID. Crude reaction mixtures were then diluted to fall within the ranged of the standard curve, yields could then be calculated (for full details see the experimental section). Results are shown in **Table 3**.

Table 3

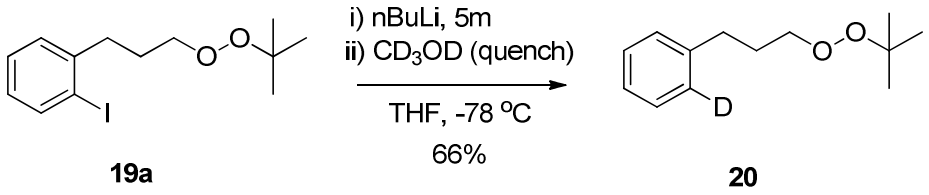


Compound	X	R	GC % Yield
19a	I	nBu	71
19a	I	Ph	73
19b	Br	nBu	71
19b	Br	Ph	47
19c	$SnBu_3$	nBu	1
19c	$SnBu_3$	Ph	19

Table 3 shows that nBuLi as well as phenyl lithium are capable of giving good yields of the desired product when X=I. However when X=Br only nBuLi gives a good yield of cyclic ether. The aryl stannane gave poor yields of the desired product, regardless of the nature of the starting organolithium.

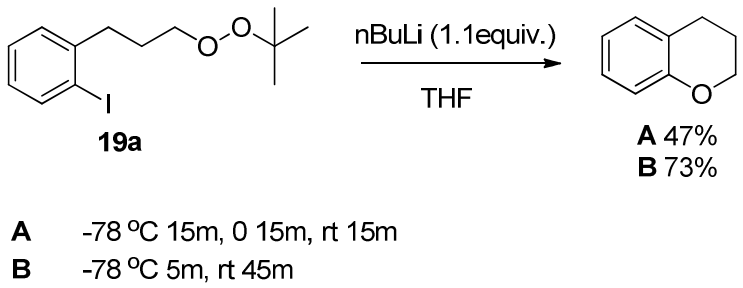
A deuterium trapping experiment was conducted to prove the existence of a organo-lithium intermediate (**Scheme 16**). At -78^{o}C, lithiation as above, followed by quenching after only 5min with CD_3OD gave compound **20** in 66% yield. The incorporation of deuterium was evident from both ^{1}HNMR and mass spectrometry. The result suggests that the organolithium intermediate is stable at -78^{o}C, with ring closure not occurring until warming.

Scheme 16: Trapping of Organo-lithium intermediate



The results on the deuterium trapping experiment were surprising as they indicated that the subsequent ring closure is sluggish at -78°C, suggesting that simply allowing the reaction to proceed at room temperature for a longer duration could result in a significant increase in yield. This was verified experimentally, as illustrated in **Scheme 17**. The conclusion here is that the final ring closure of the organo-lithium intermediate is actually quite slow. By using just one equivalent of n-butyl lithium at -78° the aryl lithium intermediate is formed efficiently. After the reaction is stirred at room temperature for 45 minutes the aryl-lithium intermediate is converted cleanly to the desired product, cyclic ether **13**.

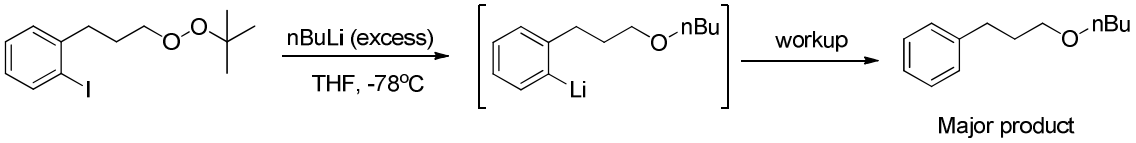
Scheme 17: Effects of temperature on the rate of ring closure



These results helped explain the results of our initial investigations, which were often conducted in the presence of excess nBuLi at -78°C. The major products in these

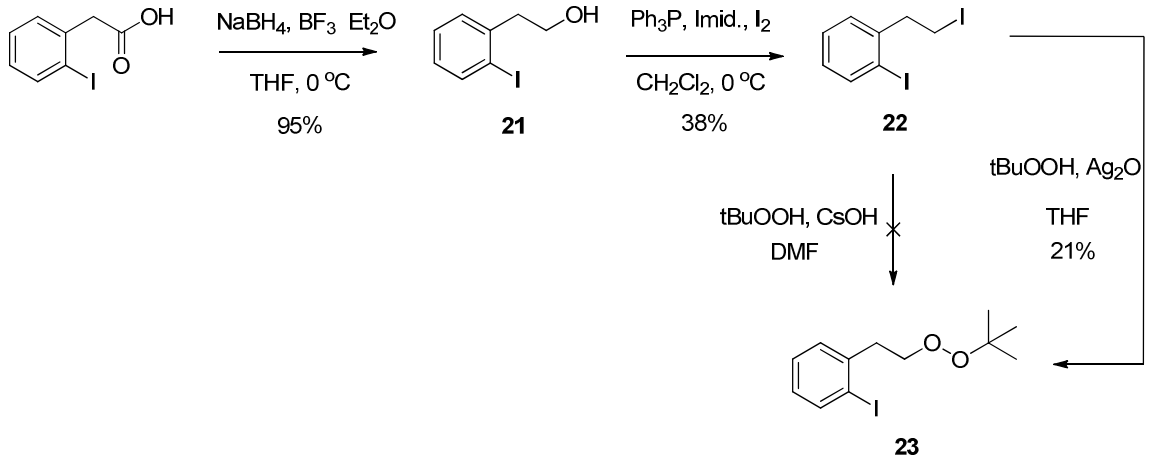
trials were dehalogenated butyl ethers. It is now clear that these conditions simply did not allow enough time for cyclization of the aryl lithium relative to the intermolecular S_N2 reaction of the peroxide with excess butyllithium. (**Scheme 18** below)

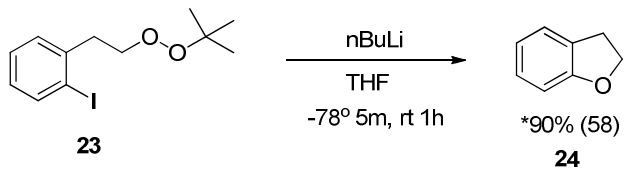
Scheme 18: Influence of excess nBuLi at -78°C



Based upon the success with the umpoled approach to a 6-member ring ether, we were interested in investigating the corresponding process of a 5-exo ring closure. The scheme below shows the synthesis of substrates as well as results of the final ring closing step.

Scheme 19





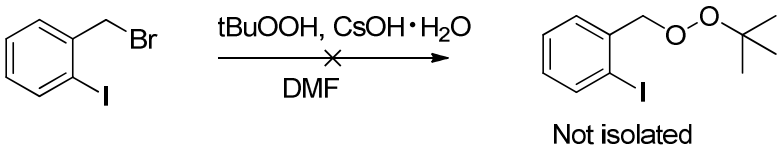
23 **24**

*GC yield (Isolated yield)

The starting halo-acid is reduced to the corresponding alcohol via a similar procedure as described for the synthesis of the 6-member ring (see **Scheme 15**). Alcohol **21** is then converted to the iodide with triphenylphosphine, imidazole, and iodine. Displacement of the iodide with tBuOOH and $CsOH•H_2O$ yielded only elimination alkene product, presumably because of the ease of E_2 elimination to form a styrene. A displacement promoted by the less basic Ag_2O gave a modest yield of halo-peroxide **23**. In the final step, compound **23** undergoes lithium/heteroatom exchange and subsequent closure to the dihydro-benzofuran in excellent yield. Due to the volatility of the product the isolated yield is significantly lower than the GC yield.

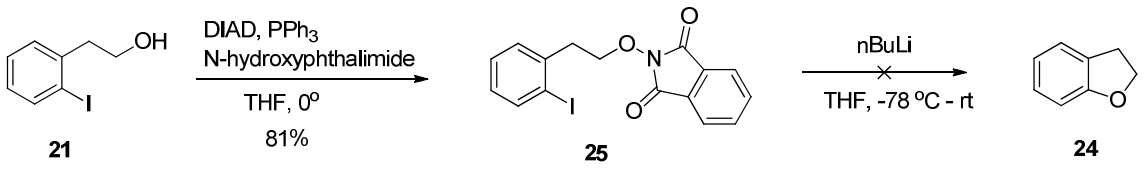
After success with formation of the 5 and 6-membered cyclic ethers, the next logical step was the preparation of a 4-membered cyclic ether. Starting from commercially available iodo-bromo compound 2-iodobenzyl bromide a displacement similar to those above was attempted. The reaction appeared to give peroxide product via TLC analysis, but the product decomposed quickly, so the product was unable to be definitively identifed and isolated. (**Scheme 20**) The presence of base may lead to elimination of the benzylic peroxide forming 2-iodobenzaldehyde and *tert*-butanol.

Scheme 20



After achieving cyclic ethers by breaking the weak O-O bond of the alkyl peroxides, we then investigated breaking an O-N bond (see **Scheme 21**). A substrate was readily prepared by a Mitsunobu reaction using diisopropyl azodicarboxylate, triphenyl phosphine and *N*-hydroxypthalimide. Unfortunately the desired C-O formation does not occur, and the reaction yields a complex mixture of unidentified products. The O-N bond is quite a bit stronger than the O-O bond, ~48 kcal/mol versus 34 kcal/mol respectively. [22] The resulting organo-lithium intermediate is likely taking other pathways to form a mixture of products. Those alternate pathways may include attack on the carbonyls or elimination of an *N*-oxide forming a styrene derivative.

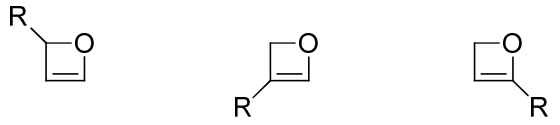
Scheme 21



After producing relatively simple benzo dihydro- furans and -pyrans we turned our attention to a class of targets that has been studied very little in the literature: oxetenes. An oxetene is a 4-membered unsaturated oxa-cycle (see example below). Oxetenes are unstable compounds that readily perform electrocyclic ring openings to

corresponding ketones and aldehydes. Due to difficulties in making and isolated oxetenes, very little investigation into these compounds has been performed. Only a limited number of methods have been reported for the synthesis of oxetenes, and few, if any, of the methods are general. A few groups have successfully made and studied a limited number of oxetenes. [23]

Scheme 22: Oxetenes

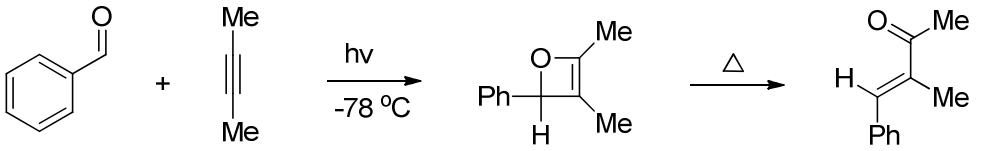


Scheme 23 below depicts previous work generating and isolating oxetenes. Irradiation of 2-butyne and benzaldehyde forms only the *E* isomer of enone **26** when the reaction is performed at -78 ^{o}C. Boeckman concluded that the enone was not formed photochemically, but was formed stereospecifically from an oxetene intermediate that then underwent electrocyclic ring opening. [23d] Attempts by Boeckman to trap the oxetene intermediate failed. Friedrich and Lam also synthesized oxetene **27** by the same method as Boeckman and reported electrocyclic ring opening to enone **26** at -40 ^{o}C. Friedrich and Lam were also were able to synthesize a more stable oxetene that was stable in solution for ~1 day. Spectral data was collected on oxetene **27** before electrocyclization to unsaturated aldehyde **28**. [23b] In a recent publication, Mikami and co-workers perform Lewis acid-promoted [2+2] cycloaddition of alkynes and ketones to isolate a number of oxetenes stabilized by a CF_3 group. The reaction is performed

between ethyl trifluoropyruvate and a large variety of alkynes catalyzed by a chiral cationic BINAP-Pd complex. Typical yields exceed 85% and 90% ee. [23a]

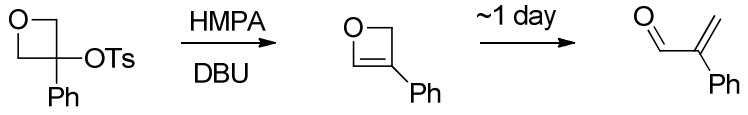
Scheme 23: Previous oxetenes

Boeckman:



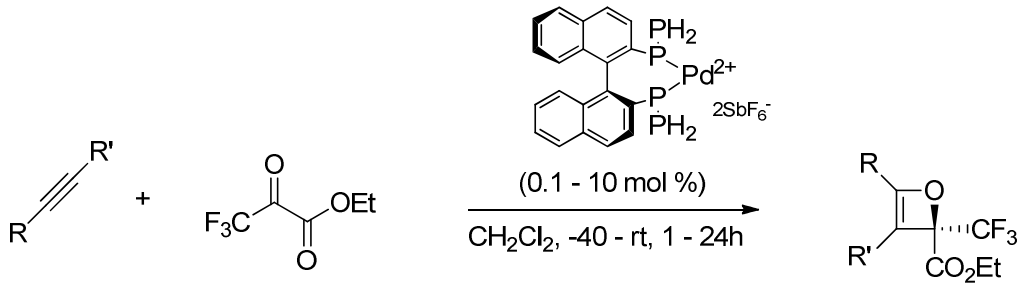
26

Friedrich and Lam:



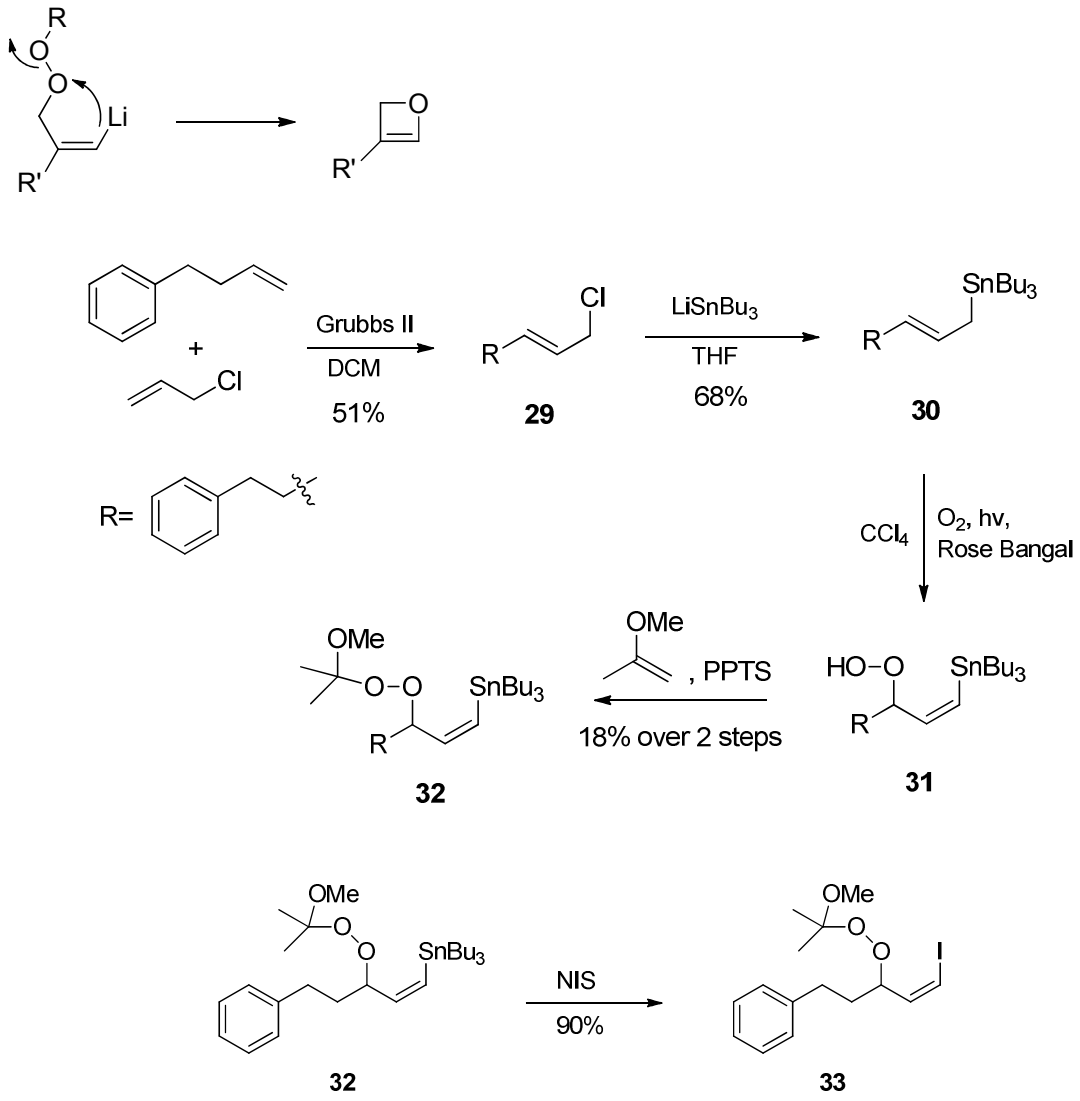
27 **28**

Mikami and coworkers:



Our approach to making oxetenes requires the synthesis of rather difficult precursors. In order to make oxetenes, we needed to synthesize a substrate capable of generating a (Z)-vinyl organo-lithium (see **Scheme 24**). Below are outlined two routes to substrates capable of undergoing lithiation to close the 4-membered oxetene ring.

Scheme 24



Stannane and iodo compounds **32** and **33** are both suitable candidates for lithium-heteroatom exchange to generate the necessary vinyl lithiums *in situ*. The goal is then to have the vinyl lithium intermediate attack the electrophilic peroxide yielding oxetenes. Synthesis of compound **32** (**Scheme 24)** begins with a cross metathesis reaction to yield the allyl chloride **29**. An attempt to perform a cross metathesis with allyl tributyltin failed

to give any of the desired product **30.** However, a straight forward displacement of the allyl chloride with $LiSnBu_3$ gave stannane **30** is good yield. In a key step, singlet oxygenation gives the (Z)-stannylhydroperoxide. Work done by previous members of our group showed that singlet oxygenations of allyl stannanes yields 3-stannyl-2-alkenyl hydroperoxides as the Z-isomer.[24] Without purification of **31,** due to difficulties isolating pure Z-stannylakenylhydroperoxide, the crude product was directly protected with 2-methoxy propene and catalytic pyridinium p-toluene sulfonate giving compound **32** in 18% yield over two steps. Stannane **32** is readily coverted to the iodo compound **33** with N-iodosuccinimide.

Another synthesis of an oxetene precursor is depicted below in **Scheme 25.** This precursor does not have a peroxyacetal, but rather a tert-butyl peroxide incorporated. The rationale for this switch was the higher intermolecular reactivity demonstrated for the peroxyacetal leaving groups. Slowing the intermolecular reaction by substituting a t-butyl peroxide for a peroxyacetal would presumably allow more time for lithium/heteroatom exchange to preceed followed by the subsequent ring closure. Unforunately the skeleton substrate used in the peroxyacetal example was unable to be used due to problems incorporating the tBuOO- functionality. We therefore chose substrate **38.** In a key step in the synthesis of this substrate commercially available propargyl alcohol **34** undergoes a hydroalumination to form intermediate **35**. The intermediate shown (**35**) accounts for the desired stereochemistry about the double bond. This intermediate is then converted *in situ* to the vinyl iodo compound **36** with iodine. The alcohol can be cleanly converted to the

diiodo compound by a similar procedure seen above. The primary iodide is then displaced by tBuOOCs in DMF to yield compound **38** in good yield.

Scheme 25

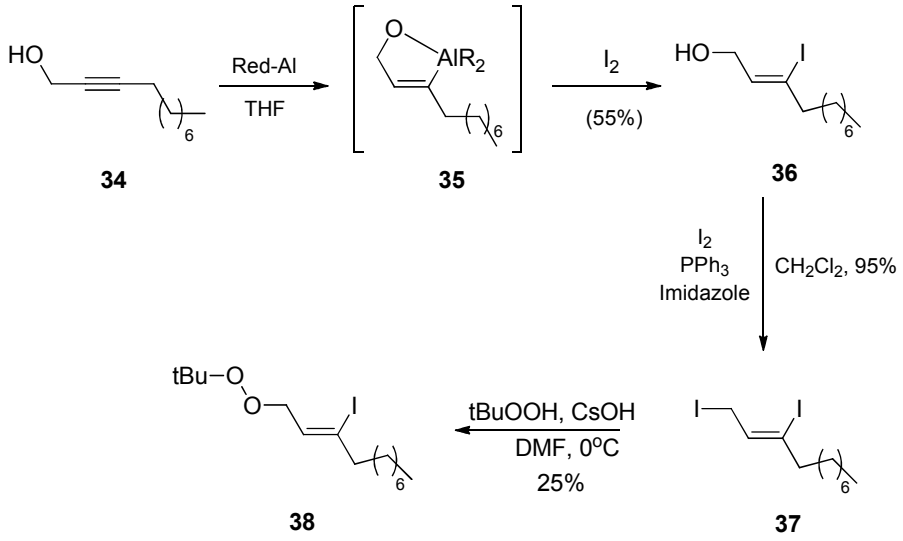


Table 4 below shows the results of subjecting substrates **32, 33,** and **38** synthesized by the above schemes to lithium/heteroatom exchange. We did not isolate oxetenes, but instead the products have undergone electrocyclic ring openings to unsaturated carbonyl compounds, shown in **Scheme 26.** The electrocyclization occurs at temperatures around -30°C. In our case, upon warming to room temperature results in complete conversion to the ring opened products. [25] Both stannane and iodo substrates were capable of generating oxetenes which then underwent electrocyclization. Entry two is a reaction conducted on a methoxypropyl peroxyacetal. In this case, we saw none of the oxetene or the ring opened unsaturated ketone product **41**; instead, we isolated the dehalogenated butyl ether. Our previous investigations (see **Table 1**) showed that methoxypropyl peroxides were much more active towards intermolecular reaction

compared with simple *tert*-butyl peroxides. We therefore synthesized a substrate in which a *tert*-butyl peroxide would serve as our electrophile. As illustrated in entries 4 and 5 of **Table 4**.

Scheme 26

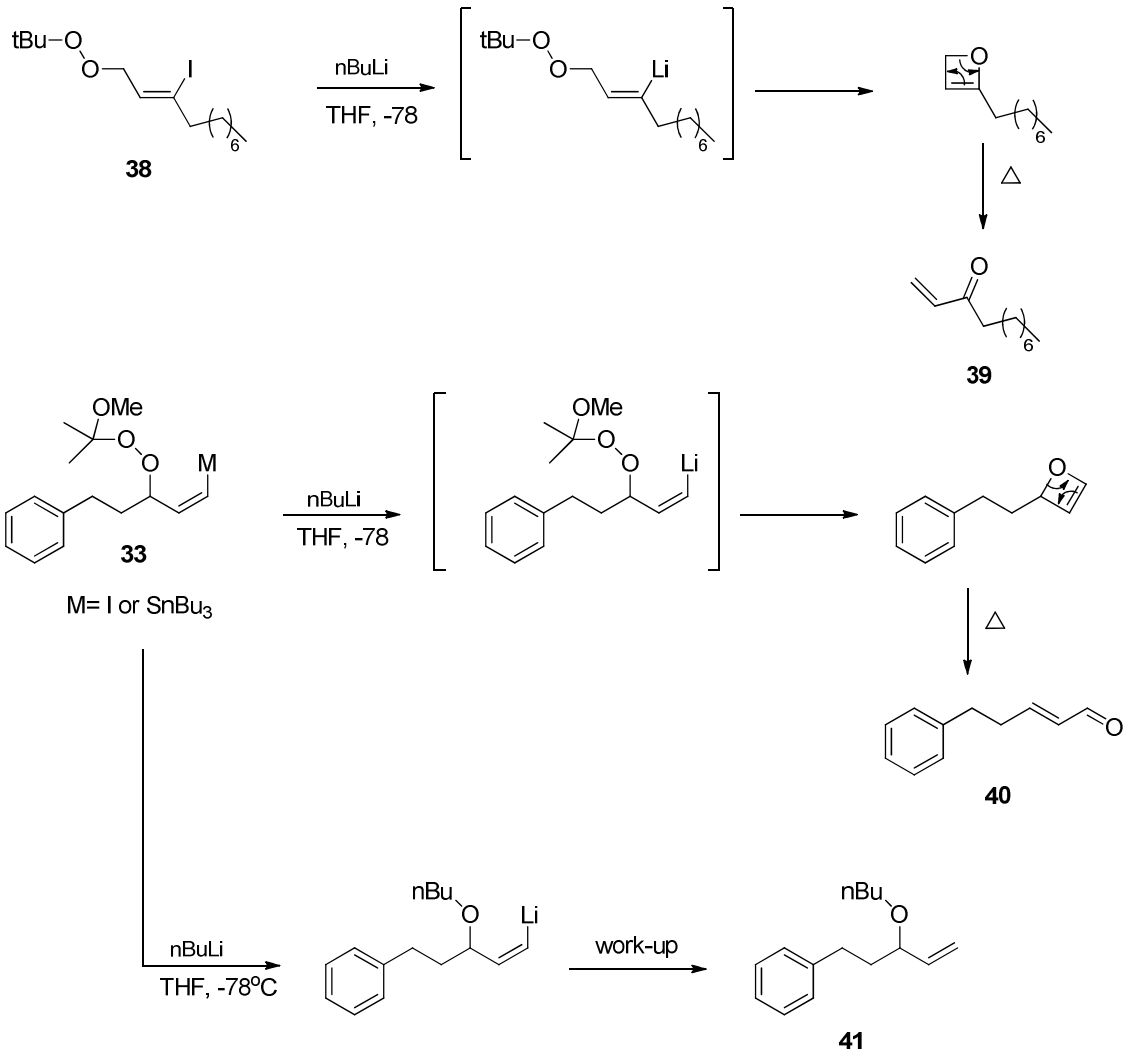
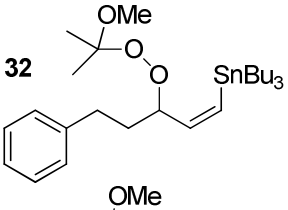
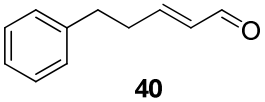
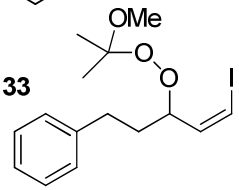
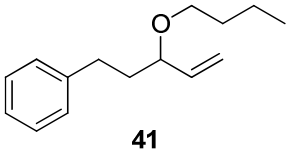
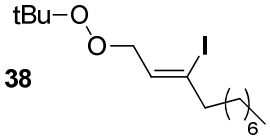
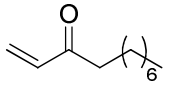
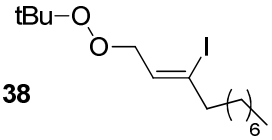


Table 4

Substrate	Temp/Time	RM (equiv.)	Product	yield (%)
32 	-78 °C / 2.5 h	nBuLi (3)	 **40**	~11
33 	-78 °C / 2.25 h	nBuLi (5)	 **41**	33
38 	-78 °C / 30 min	nBuLi (2)	 **39**	*
38 	-78 °C / 15 min	tBuLi (2.5)	-	0

*Product was not able to be isolated, but was seen in crude ^{1}H NMR

Many of the trials related to oxetenes were conducted before we became aware of the low rate of cyclization in the 6-membered ring model system. The oxetene closure is likely as slow or slower than the 6-member closure seen prior in this chapter. In hindsight, the efficiency of these reactions could have been increased by warming the reactions after lithiation with only one equivalent of *n*BuLi. The reactions for the oxetenes were performed at -78 °C and then quenched. By simply allowing for the vinyl-

lithium intermediate to warm up, I believe more efficient closure of the 4-member oxetene ring could be achieved. After depositing of this thesis to the library, some of these attempts will be investigated.

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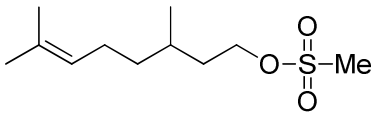
Experimental Section

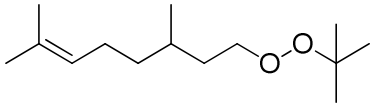
All solvents and reagents were bought from commercially available sources and used without further purification except for THF and CH_2Cl_2, which were distilled from sodium/benzophenone and calcium hydride respectively. Reaction vials or flasks were equipped with magnetic stir bars, flame dried prior to use, and purged with nitrogen. Reactions were then performed under nitrogen while stirring. Thin layer chromatography (TLC) was performed on 0.25 mm hard-layer silica G plates; developed plates were visualized with a UV lamp or by staining: 1% ceric sulfate and 10% ammonium molybdate in 10% H_2SO_4 (general stain after charring); 1% *N,N'* – dimethyl-p-phenylenediamine solution in 1:20:100 acetic acid/water/methanol (specific for peroxides); 1% aqueous potassium permanganate (for unsaturated compounds); 3% vanillin in 3% H_2SO_4 in ethanol (general stain after charring). ^{1}H NMR and ^{13}C NMR spectra were aquired in $CDCl_3$ on a Bruker Advance 600 MHz NMR, Bruker Advance 400 MHz NMR, or Bruker 300 MHz NMR. ^{1}H NMR spin systems are reported as: ppm (multiplicity, integration, J coupling where relevant). Infrared spectra were performed with neat films (ZnSe, ATR mode) with selected absorbances reported in wavenumbers (cm^{-1}). GC-FID work was performed on a Varian CP-3380 with a DB5 column.

Abbriviations: tetrahydrofuran (THF), hexanes (Hex), ethyl acetate (EA), dimethylformamide (DMF), diethyl ether (ether)



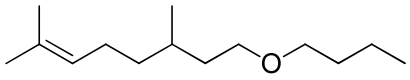
3,7-dimethyloct-6-en-1-ol methansulfonate (1)

A 0.12M solution of citronellol (467 mg, 3.0 mmol) in methylene chloride at 0 ^{o}C was added Et_3N (1.25 mL, 9 mmol) followed by methanesulfonyl chloride (0.35 mL, 0.35 mmol) slowly. The reaction was allowed to warm slowly to room temperature and stirred for 16 h. The reaction was quenched with 25 mL of water and extracted with methylene chloride. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by column chromatography (25% EA/Hex) to yield 662 mg (94%) of the title compound as a light yellow oil. R_f: 0.5 (25% EA/Hex). ^{1}H NMR (400 MHz): δ 0.95 (d, 3H, J= 6.5), 1.22 (m, 1H), 1.36 (m, 1H), 1.51-166 (singlet overlapping unresolved signal, 5H), 1.70 (d, 3H, J= 0.9), 1.80 (m, 1H), 1.99 (m, 2H), 3.02 (s, 3H), 4.27 (m, 2H), 5.09 (app. triplet of quintets, 1H, J= 7.1, 1.4). ^{13}C NMR (100 MHz): δ 17.7 (CH_3), 19.2 (CH_3), 25.3 (CH_3), 25.7 (CH_2), 28.9 (CH), 35.9 (CH_2), 36.8 (CH_2), 37.4 (CH_3), 68.6 (CH_2), 124.3 (CH), 131.6 (C). CAS#: 42602-37-9 The spectra matched those previously reported for this molecule. (Vincent G., Bulletin of the Chem. Soc. of Japan 2009, Vol. 82 (7), pp. 829-842.



3,7-dimethyloct-6-en-1-yl *tert*-butyl peroxide (2)

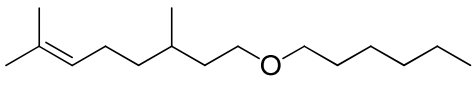
To a suspension of CsOH monohydrate (6.76 g, 40 mmol) in DMF (80 mL) at 0 ^{o}C was added tBuOOH (8.8 mL, 48 mmol, of a 5.5 M solution in decane) slowly. The mixture was allowed to stir for 30 min, then methanesulfonate **1** (6.3 g, 27 mmol) was added dropwise in 5 mL of DMF. The reaction was allowed to slowly warm to room temperature. After 5 h, 50 mL of water was added and the resulting mixture was extracted with ether. The combined organic layers were washed with brine and dried with Na_2SO_4. The reside was concentrated under reduced pressure and purified by column chromatography (2.5% EA/Hex) to yield 3.9g (64%) of the title compound as a colorless oil. R_f: 0.65 (10% EA/Hex). ^{1}H NMR (400 MHz): δ 0.92 (d, 3H, J= 6.6), 1.18 (m, 1H), 1.26 (s, 9H), 1.30-1.47 (2H, unresolved overlapping signals), 1.50-1.68 (singlet overlapping unresolved signal, 5H), 1.70 (d, 3H, J= 0.9), 1.99 (m, 2H), 3.99 (m, 2H), 5.11 (app. triplet of quintets, 1H, J= 7.2, 1.4). ^{13}C NMR (100 MHz): δ 17.6 (CH_3), 19.6 (CH_3), 25.4 (CH_3), 25.7 (CH_2), 26.3 (tBu CH_3's), 29.7 (CH), 34.6 (CH_2), 37.1 (CH_2), 73.4 (CH_2), 80.0 (C), 124.7 (CH), 131.2 (C). IR: 2975, 2927, 2873, 1456, 1377, 1361, 1241, 1197, 884.



3,7-dimethyloct-6-en-1-yl butyl ether (4)

To a 0.2 M solution of peroxide **2** (234 mg, 1.0 mmol) in THF at -78 ^{o}C was added nBuLi (0.80 mL, 2.0 mmol of a 2.5 M solution in hexane) drop wise. After 10 min the reaction was warmed to room temperature. After 4 h the reaction was quenched with 5 mL of

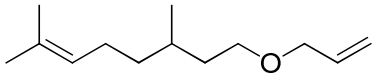
water and extracted with ether. The organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by column chromatography (2.5% EA/Hex) to yield 138 mg (63%) of the title compound as a colorless oil. R_f: 0.5 (10% CH_2Cl_2/Hex). ^{1}H NMR (400 MHz): δ 0.89-0.97 (s and d overlapping, 6H), 1.18 (m, 1H), 1.30-1.47 (overlapping signals, 4H), 1.52-1.67 (singlet overlapping with 2 other signals, 7H), 1.70 (d, J= 1.0), 2.00 (m, 2H), 3.36-3.51 (overlapping signals, 4H), 5.12 (app. triplet of quintets, J= 7.2, 1.3). ^{13}C NMR (100 MHz): δ 13.9 (CH_3), 17.6 (CH_2), 19.4 (CH_3), 19.6 (CH_3), 25.5 (CH_2), 25.7 (CH_3), 29.6 (CH), 31.9 (CH_2), 36.7 (CH_2), 37.2 (CH_2), 69.2 (CH_2), 70.7 (CH_2), 124.9 (CH), 131.1 (C). IR: 2959, 2926, 2856, 1256, 1376, 1131, 830, 737.



3,7-dimethyloct-6-en-1-yl hexyl ether (5)

To a 0.2 M solution of peroxide **2** (230 mg, 1.0 mmol) in THF at -78 ^{o}C was added hexylMgBr (1.5 mL of a 2 M solution in diethylether, 3.0 mmol). After 10 min the reaction was allowed to warm to room temperature and stir for 8 h. The reaction was then quenched with 5 mL of water and extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude was then purified by column chromatography (5% EA/Hex) to yield 99.8 mg (42%) of the title compound as a colorless oil. R_f: 0.5 (5%EA/Hex). ^{1}H NMR (400 MHz): δ 0.83-0.96 (t and d overlapping, 6H), 1.18 (m, 1H), 1.25-1.46 (8H), 1.50-1.66 (singlet overlapping with 2

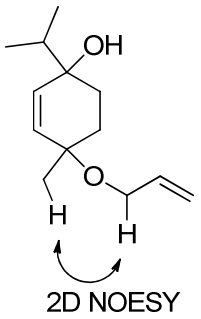
other signals, 7H), 1.70 (s, 3H), 2.00 (m, 2H), 3.33-3.52 (overlapping signals, 4H), 5.12 (app. triplet of quintets, 1H, J= 7.1, 1.3). ^{13}C NMR (100 MHz): δ 14.0 (CH_3), 17.6 (CH_3), 19.6 (CH_3), 22.6 (CH_2), 25.5 (CH_2), 25.7 (CH_2), 25.9 (CH_3), 29.6 (CH_2), 29.8 (CH), 36.7 (CH_2), 37.2 (CH_2), 69.2 (CH_2), 71.0 (CH_2), 124.9 (CH), 131.1 (C).



3,7-dimethyloct-6-en-1-yl allyl ether (6)

To a 0.2 M solution of peroxide **2** (229 mg, 1.0 mmol) in THF was added allyltributyl tin (0.62 mL, 2.0 mmol). The solution was cooled to -78 ^{o}C, and nBuLi (2.5 mmol, 1.0 mL of a 2.5 M solution in hexane) was added drop wise. After 30 min the reaction was quenched with 10 mL of water and extracted with ether. The combined organic layer was dried with Na_2SO_4, and concentrated under reduced pressure. The residue was then purified by column chromatography (2.5% EA/Hex) to yield 137 mg (70%) of the title compound as a colorless oil. R_f: 0.25 (5% EA/Hex). ^{1}H NMR (400 MHz): δ 0.92 (d, 3H, J= 6.7), 1.18 (m, 1H), 1.39 (m, 1H), 1.52-1.68 (singlet at 1.62 overlapping unresolved signal, 5H), 1.70 (s, 3H), 2.00 (m, 2H), 3.48 (m, 2H), 3.98 (dt, 2H, J= 5.6, 1.4), 5.12 (triplet of septets, 1H, J= 7.1, 1.4), 5.19 (app. dq, H_{cis}, J= 10.6, 1.3), 5.29 (app. dq, H_{trans}, J= 17.2, 1.6), 5.94 (ddt, 1H, J= 17.2, 10.3, 5.6), 5.94 (tdd, 1H, J= 13.8, 10.5, 5.6). ^{13}C NMR (100 MHz): δ 17.6 (CH_3), 19.6 (CH_3), 25.5 (CH_3), 25.7 (CH_2), 29.6 (CH), 36.7 (CH_2), 37.2 (CH_2), 68.7 (CH_2), 71.8 (CH_2), 99.9 (vinyl CH_2), 116.7 (vinyl CH), 124.8 (vinyl CH), 131.2 (vinyl C), 135.1 (vinyl CH). Spectra matched those previously

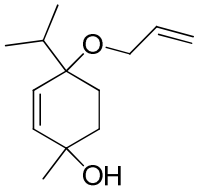
reported for this molecule. CAS:139694-24-9 (Banerjee, S., Balasanthiran, V., Koodali, R. T., Sereda, G. A., Organic & Biomolecular Chemistry (2010), 8(19), 4316-4321)



4-(allyloxy)-1-isopropyl-4-methylcyclohex-2-enol (7)

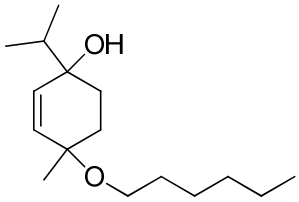
To a 0.2 M solution of ascaridole (168 mg, 1.0 mmol) at 0 ^{o}C was added allylMgCl (3 mmol, 1.5 mL of a 2 M solution in THF) drop wise. After 15 min the reaction was quenched with 10 mL of water and extracted with ether. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by column chromatography (20% EA/Hex) to yield 38 mg (21%) of the title compound as a colorless oil. A 2-d NOE experiment showed energy transfer between the two protons shown above, successfully identifying the two regio-isomers formed in the reaction. R_f: 0.25 (20% EA/Hex). ^{1}H NMR (300 MHz): δ 0.91 (d, 3H, J= 7.0), 0.97 (d, 3H, J= 6.8), 1.26 (s, 3H), 1.49 (s, 1H), 1.62 (m, 1H), 1.67-1.80 (overlapping signals, 3H), 2.16 (m, 2H), 3.98 (dt, 2H, J= 12.5, 1.5), 5.15 (app. dq, $1H_{cis}$, J= 10.4, 1.5), 5.30 (app. dq, $1H_{trans}$, J= 17.2, 1.8), 5.67 (dd, 1H, J= 10.2, 1.1), 5.73 (dd, J= 10.2, 1.5), 5.94 (ddt, 1H, J= 17.2, 10.3, 5.4). ^{13}C NMR (100 MHz): δ 16.3 (CH_3), 17.5 (CH_3), 25.0 (CH_3),

28.6 (CH_2), 29.3 (CH_2), 37.4 (CH), 63.7 (CH_2), 71.6 (C), 74.8 (C), 115.9 (CH_2), 133.4 (CH), 136.0 (CH), 136.1 (CH). HRMS (ESI): calcd for $C_{11}H_{22}O_2$ $(M+Na)^+$: 233.1517; found: 233.1517. IR: 3420, 2959, 2873, 1463, 1367, 1220, 1122, 1058, 1008, 915, 772.



(8)

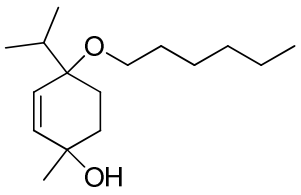
This molecule was not able to be purified.



4-(hexyloxy)-1-isopropyl-4-methylcyclohex-2-enol (9)

To a 0.2 M solution of ascaridole (165 mg, 0.98 mmol) at 0 ^oC was added hexylMgBr (3mmol, 1.5mL of a 2 M solution in THF) drop wise. After 15 min the reaction was quenched with 10 mL of water and extracted with ether. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by column chromatography (20% EA/Hex) to yield 60 mg (24%) of the title

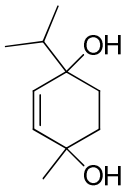
compound as a colorless oil. R_f: 0.20 (20% EA/Hex). ^{1}H NMR (400 MHz): δ 0.87-0.94 (overlapping signals, 6H), 0.97 (d, 3H, J= 6.6), 1.22 (s, 3H), 1.25-1.40 (6H), 1.48-1.65 (overlapping signals, 4H), 1.68-1.79 (overlapping signals, 3H), 2.13 (tt, 1H, J= 12.0, 12.0), 3.39 (m, 2H), 5.64 (dd, 1H, J= 10.3, 1.2), 5.71 (dd, 1H, J= 10.3, 1.5). ^{13}C NMR (100 MHz): δ 14.1 (CH_3), 16.3 (CH_3), 17.5 (CH_3), 22.7 (CH_2), 24.9 (CH_2), 25.9 (CH_2), 28.6 (CH_2), 29.2 (CH_3), 30.7 (CH_2), 31.8 (CH_2), 37.3 (CH), 62.3 (CH_2), 71.6 (CH), 73.9 (CH), 139.9 (CH), 136.6 (CH). Schwaebe, M. K., Little, R. D., Tetrahedron Letters, Vol. 37, No. 37, pp. 6635-6638, 1996. HRMS (ESI): calcd for $C_{16}H_{30}O_2$ $(M+Na)^+$: 277.2143; found: 277.2144. IR: 3418, 2956, 2929, 2859, 2361, 1465, 1383, 1365, 1301, 1123, 1107, 1069, 1007, 939, 905, 771, 664. This molecule was previously reported without characterization: Schwaebe, M. K., Little, R. D., Tetrahedron Letters, Vol. 37, No. 37, pp. 6635-6638, 1996.



4-(hexyloxy)-4-isopropyl-1-methylcyclohex-2-enol (10)

Compound **10** was synthesized in the same reaction as compound **9** and **11**. The compounds eluded during purification by column chromatography in the following order: **10**, **9**, **11**. Elution of the **10** was achieved with 20% EA/Hex to give 25 mg (10%) of the title compound as a colorless oil. R_f: 0.25 (20% EA/Hex). ^{1}H NMR (400 MHz): δ 0.85

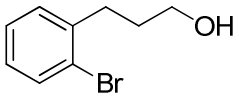
(d, 3H, J= 6.8), 0.87-0.94 (overlapping signals, 6H), 1.24-1.40 (singlet overlapping 3 CH_2's, 9H), 1.47-1.66 (overlapping signals 4H), 1.76 (m, 2H), 1.92 (m, 2H), 3.34 (t, 2H, J= 6.7), 5.55 (dd, 1H, J= 10.3, 1.1), 5.83 (dd, 1H, J= 10.3, 1.0). ^{13}C NMR (100 MHz): δ 14.1 (CH_3), 16.3 (CH_3), 17.6 (CH_3), 22.6 (CH_2), 25.9 (CH_2), 26.0 (CH_2), 27.2 (CH_2), 30.7 (CH_3), 31.7 (CH_2), 33.7 (CH_2), 35.1 (CH), 61.9 (CH_2), 69.4 (CH), 75.4 (CH), 131.1 (CH), 138.2 (CH). HRMS (ESI): calcd for $C_{16}H_{30}O_2$ $(M+Na)^+$: 277.2143; found: 277.2144. IR: 3351, 2957, 2929, 2858, 2359, 1465, 1382, 1231, 1202, 1122, 1080, 1033, 1004, 952, 917, 896, 770, 736, 710, 659. This molecule was previously reported without characterization: Schwaebe, M. K., Little, R. D., Tetrahedron Letters, Vol. 37, No. 37, pp. 6635-6638, 1996.



1-isopropyl-4-methylcyclohex-2-ene-1,4-diol (11)

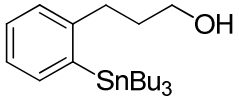
Compound **11** was synthesized in the same reaction as compound **7** and **8**. The compounds eluded during purification by column chromatography in the following order: **8**, **7**, **11**. Elution of the **11** was achieved with 60% EA/Hex to give 95 mg (60%) of the title compound as a colorless oil. R_f: 0.40 (60% EA/Hex). ^1H NMR (400 MHz): δ 0.86 (d, 3H, J= 7.3), 0.92 (d, 3H, J= 6.9), 1.21 (s, 3H), 1.59-1.78 (overlapping signals, 4H), 1.92 (m, 1H), 2.63 (s, 1H), 3.16 (s, 1H), 5.50 (dd, 1H, J= 10.0, 1.1), 5.67 (dd, 1H, J= 10.0,

1.2). ^{13}C NMR (100 MHz): δ 16.4 (CH_3), 17.5 (CH_3), 27.0 (CH_3), 28.8 (CH_2), 34.6 (CH_2), 37.1 (CH), 69.4 (CH), 71.8 (CH), 131.7 (CH), 137.1 (CH). CAS#: 4031-37-2 (Valente, P.; J. Org. Chem. 2009, vol. 74(1), pg. 274-282)



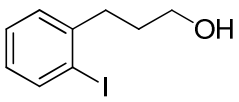
3-(2-Bromophenyl)propanol (14)

To a 0.5 M solution of commercially available 3-(2-bromophenyl)propionic acid (771 mg, 3.37 mmol) in THF at 0 ^oC was added $NaBH_4$ (255 mg, 6.7 mmol) in one portion. BF_3 etherate (0.842 mL, 6.7 mmol) was then added dropwise and the reaction stirred for 1 hour. The reaction was quenched with methanol (4 mL) followed by 1M HCl (4 mL). The mixture was diluted with EtOAc (15 mL) and the separated organic layer was dried with Na_2SO_4 and concentrated under reduced pressure. The crude mixture was purified by flash chromatography (30% EA/Hex) to yield 668 mg (92%) of the title compound as a colorless oil. R_f : 0.33 (30% EA/Hex); ^1H NMR (300 MHz): δ 1.91 (tdd, 2H J= 8.0, 7.9, 6.4), 2.86 (m, 2H), 3.71 (t, 2H, J= 6.3), 7.02-7.13 (m, 1H), 7.20-7.30 (m, 2H), 7.55 (d, 1H, J= 7.8). ^{13}C NMR (75 MHz): δ 32.4 (CH_2), 32.7 (CH_2), 62.1(CH_2), 124.5 (C), 127.5 (CH), 127.7 (CH), 130.4 (CH), 132.8 (CH), 141.1 (C). Spectra matched those previously reported for this molecule. (J. Am. Chem. Soc. 2003, 125, 3509-3521).



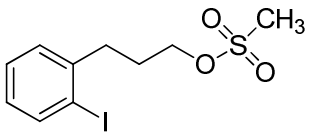
3-(2-(Tributylstannyl)phenyl)propan-1-ol (15)

To a 0.1 M solution of 3-(2-bromophenyl)propan-1-ol **14** (0.5 mmol, 104 mg) in THF at -78 ^{o}C was added nBuLi (1.6 M / Hex, 1.1 mmol, 0.69 mL) slowly drop wise. The mixture was stirred for 10 minutes at -78 ^{o}C, then tributyltin chloride (1.1 mmol, 0.30 mL) was added. The reaction was then allowed to warm slowly up to room temperature. After 5 hours the reaction was quenched with water and sat. aq. NH_4Cl, extracted with ether, and dried with Na_2SO_4. The mixture was concentrated under reduced pressure and purified via column chromatography (10% EA/Hex) to yield 126 mg (59%) of the title compound as a colorless oil. R_f : 0.40 (20% EA/Hex); ^{1}H NMR (400 MHz): δ 0.91 (t, 9H, J= 7.3), 1.10 (m, 6H), 1.35 (m, 6H), 1.53 (m, 6H), 1.90 (m, 2H), 2.70 (m, 2H), 3.76 (dd, 2H, J= 11.3, 6.2), 7.12-7.50 (m, 5H). ^{13}C NMR (100 MHz): δ 10.4 (CH_3), 13.7 (CH_2), 27.4 (CH_2), 29.2 (CH_2), 35.2 (CH_2), 35.4 (CH_2), 62.7 (CH_2), 125.4 (CH), 128.0 (CH), 128.4 (CH), 136.9 (C), 141.8 (CH), 148.6 (C). HRMS (ESI): calcd for $C_{21}H_{38}OSn$ $(M+Na)^+$: 449.1742; found: 449.1845. IR: 3332, 3051, 2953, 2921, 2870, 2851, 1463, 1433, 1417, 1375, 1339, 1291, 1151, 1056, 959, 864, 749, 662, 589.



3-(2-Iodophenyl)propanol (16)

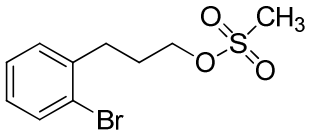
To a 0.42 M solution of commercially available 3-(2-iodophenyl)propionic acid (2.926 g, 10.6 mmol) in THF was added $NaBH_4$ at 0 ^oC (825 mg, 21.8 mmol) in one portion. BF_3 etherate (2.74 mL, 21.8 mmol) was then added drop wise and the reaction and stirred for 1 hour. The reaction was quenched with 12 mL MeOH followed by 12 mL 1M HCl. The mixture was then diluted with EtOAc and the organic layer separated and dried with Na_2SO_4. The resulting solution was concentrated under reduced pressure and the residue purified by flash chromatography (30% EA/Hex) to yield 2.63g (95%) of the title compound as a light yellow oil. R_f : 0.33 (30% EA/Hex); ^1H NMR (400 MHz): δ 1.89 (tdd, 2H, J= 6.3, 9.6, 6.3), 2.83 (m, 2H), 3.73 (t, 2H, J= 6.5), 6.90 (ddd, 1H J= 8.3, 7.5, 2.0), 7.20-7.35 (m, 2H), 7.83 (dd, 1H, J= 8.1, 1.1). ^{13}C NMR (100 MHz): δ 33.1 (CH_2), 37.0 (CH_2), 62.1(CH_2), 100.61 (C), 127.8 (CH), 128.4 (CH), 129.5 (CH), 139.5 (CH), 144.4 (C). Spectra matched those previously reported for this molecule. (Tummatorn, J., Dudley, G. B., Org. Lett., Vol. 13, No. 6, 2011, 1572-1575).



3-(2-Iodophenyl)propyl methansulfonate (18a)

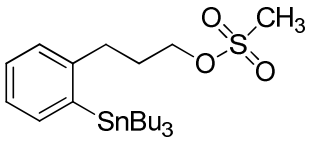
Alcohol **16** (1.78 g, 5.23 mmol) was converted to the corresponding methanesulfonate by the same procedure employed for compound **18b** to yield 2.14g (92%) of the title compound as a light yellow oil. R_f: 0.5 (30% EA/Hex). ^1H NMR (400 MHz): δ 2.10 (m, 2H), 2.88 (t, 2H, J= 7.7), 4.30 (t, 2H, J= 6.3), 6.94 (td, 1H, J= 7.6, 1.8), 7.25 (dd, 1H, J=

7.7, 1.8), 7.32 (td, 1H, J= 7.4, 1.2), 7.85 (dd, 1H, J= 7.9, 1.2). Spectra matched those previously reported for this molecule. (Minatti, A., Buchwald, S. L., Org. Lett., Vol. 10, No. 13, 2008, 2721-2724).



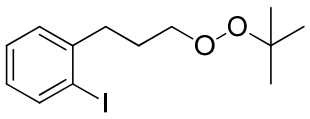
3-(2-Bromophenyl)propyl methanesulfonate (18b)

To a 0.2 M solution of alcohol **14** (1.83 g, 8.51 mmol) in methylene chloride was added Et_3N (4.7 mL, 34 mmol) followed by methanesulfonyl chloride (0.99 mL, 12.8 mmol) drop wise at 0 ^oC. The resulting mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched with 20 mL of water. Extraction was performed with additional methylene chloride (2 X 30 mL) and the combined organic layers were dried with Na_2SO_4. The crude mixture was concentrated under reduced pressure and purified by flash chromatography (20% EA/Hex) to yield 2.24 g (90%) of the title compound as a light yellow oil. R_f: 0.45 (20% EA/Hex). ^1H NMR (400 MHz): δ 2.11 (tdd, 2H, J= 7.8, 7.0, 6.3), 2.90 (m, 2H), 3.04 (s, 3H), 4.28 (t, 2H J= 6.3), 7.05-7.15 (m, 1H), 7.20-7.32 (m, 2H), 7.56 (dd, 1H, J= 8.1, 0.9). ^{13}C NMR (100 MHz): δ 29.1 (CH_2), 32.1 (CH_2), 37.5 (CH_3), 69.0(CH_2), 124.4 (C), 127.7 (CH), 128.2 (CH), 130.6 (CH), 133.0 (CH), 139.7 (C). HRMS (ESI): calcd for $C_{10}H_{13}BrO_3S$ $(M+Na)^+$: 314.9666; found: 314.9659. IR: 2940 (w), 1567 (w), 1471, 1439, 1348, 1169, 1021, 969, 920, 835, 810, 750, 728, 657.



3-(2-(Tributylstannyl)phenyl)propyl methansulfonate (18c)

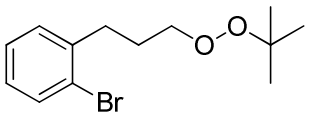
Alcohol **15** (42.5 mg, 0.10 mmol) was converted to the corresponding methanesulfonate by the same procedure employed for compound **18b** to yield 31.7 mg (63%) of the title compound as a colorless oil. R_f: 0.6 (30% EA/Hex). ^{1}H NMR (400 MHz): δ 0.91 (t, 9H J= 7.3),1.10 (m, 6H), 1.36 (quintet, 6H, J= 7.3), 1.53 (m, 6H), 2.07 (tdd, 2H, J= 7.3, 9.8, 6.4), 2.74 (m, 2H), 3.04 (s, 3H), 4.31 (t, 2H, J= 6.5), 7.15-7.35 (m, 4H), 7.35-7.50 (m, 1H). ^{13}C NMR (100 MHz): δ 10.4 (CH_3), 13.7 (CH_2), 27.4 (CH_2), 29.1 (CH_2), 31.5 (CH_2), 34.9 (CH_2), 37.4 (CH_3), 69.2 (CH_2), 125.7 (CH), 127.9 (CH), 128.5 (CH), 137.1 (CH), 141.9 (C), 147.2 (C). HRMS (ESI): calcd for $C_{22}H_{40}O_3SSn$ $(M+Na)^+$: 527.1618; found: 527.1619. IR: 2954, 2921, 2870, 2851, 1463, 1355, 1173, 1072, 1000, 959, 921, 873, 833, 806, 751, 730, 667, 591.



2-Iodophenyl-1-propyl *tert*-butyl peroxide (19a)

Methanesulfonate **18a** (2.14 g, 6.30 mmol) was converted to the corresponding peroxide by the same procedure employed in compound **19b** to yield 1.61 g (77%) of the title

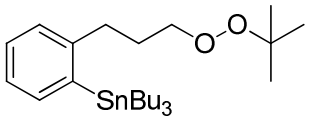
compound as a light yellow oil. R_f: 0.45 (5% EA/Hex). ^{1}H NMR (400 MHz): δ 1.23 (s, 9H), 1.94 (tdd, 2H, J= 6.4, 9.0, 6.5), 2.82 (m, 2H), 4.03 (t, 2H, J= 6.4), 6.90 (td, 1H, J= 7.4, 1.9), 7.27 (m, 2H), 7.83 (dd, 1H, J= 7.8, 1.1). ^{13}C NMR (100 MHz): δ 26.4 (CH_3), 28.4 (CH_2), 37.4 (CH_2), 74.0 (CH_2), 80.1 (C), 100.6 (C), 127.8 (CH), 128.3 (CH), 129.4 (CH), 139.5 (CH), 144.3 (C). HRMS (ESI): calcd for $C_{13}H_{19}IO_2$ $(M+Na)^+$: 357.0327; found: 357.0315. IR: 2975, 2867, 1562, 1465, 1434, 1361, 1240, 1195, 1079, 1048, 1008, 876, 746, 646.



2-Bromophenyl-1-propyl *tert*-butyl peroxide (19b)

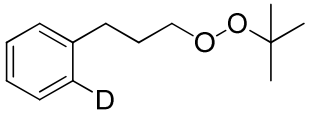
To a suspension of $CsOH•H_2O$ (2.52 g) in DMF (25 mL) was added tBuOOH (5.5 mL of a 5.5 M solution in Decane) at 0 ^oC. After stirring for 10 minutes, methanesulfonate **18b** (2.29 g, 7.8 mmol) was added in 5 mL of DMF. The reaction was allowed to warm slowly to room temperature and stirred for 5 hours. The reaction was then quenched with 10 mL of water and 10 mL of sat. aq. NH_4Cl. The ether extract was dried with Na_2SO_4 and concentrated under reduced vacuum. The crude mixture was then purified via column chromatography (2.5% EA/Hex) to yield 897 mg (42%) of the title compound as a colorless oil. R_f: 0.45 (5% EA/Hex). ^{1}H NMR (400 MHz): δ 1.29 (s, 9H), 1.97 (tdd, 2H, J = 7.0, 9.7, 6.4), 2.84 (m, 2H), 4.02 (t, 2H, J= 6.5), 7.07 (m, 1H), 7.26 (m, 2H), 7.55 (d, 1H, J= 7.9). ^{13}C NMR (100 MHz): δ 26.4 (CH_3), 28.0 (CH_2), 32.8 (CH_2), 74.1 (CH_2),

80.1 (C), 124.5 (C), 127.4 (CH), 127.6 (CH), 130.4 (CH), 132.8 (CH), 141.1 (C). HRMS (ESI): calcd for $C_{13}H_{19}BrO_2$ $(M+Na)^+$: 309.0466; found: 309.0457. IR: 2975, 2869, 2358, 1470, 1438, 1384, 1361, 1240, 1195, 1019, 877, 746, 657.



2-(Tributylstannyl)phenyl-1-propyl *tert*-butyl peroxide (19c)

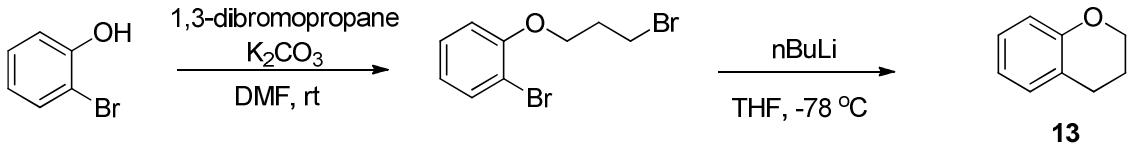
Methanesulfonate **18c** (418 mg, 0.83 mmol) was converted to the corresponding peroxide by the same procedure employed for compound **19b** to yield 246 mg (60%) of the title compound**.** R_f: 0.5 (5% EA/Hex). ^{1}H NMR (400 MHz): δ 0.91 (t, 9H, J= 7.3), 1.1 (m, 6H), 1.29 (s, 9H), 1.36 (quintet, 6H, J= 7.3), 1.54 (m, 6H), 1.93 (m, 2H), 2.70 (m, 2H), 4.05 (t, 2H, J= 6.5), 7.01-7.33 (m, 3H), 7.41 (m, 1H). ^{13}C NMR (100 MHz): δ 10.4 (CH_3), 13.7 (CH_2), 26.4 (CH_3), 27.4 (CH_2), 29.2 (CH_2), 30.5 (CH_2), 35.9 (CH_2), 74.6 (CH_2), 80.1 (C), 125.3 (CH), 127.9 (CH), 128.4 (CH), 136.8 (CH), 141.8 (C), 148.6 (C). HRMS (ESI): calcd for $C_{25}H_{45}O_2Sn$ $(M+Na)^+$: 521.2417; found: 521.2430. IR: 3051, 2955, 2922, 2870, 2852, 2360, 1463, 1434, 1375, 1361, 1241, 1196, 1071, 1020, 959, 875, 750, 667, 592.



2-Deuterophenyl-1-propyl *tert*-butyl peroxide (20)

A 0.2 M solution of peroxide (**19a**) (66.5 mg, 0.2 mmol) in THF was cooled to -78°C. A 1.6 M solution of nBuLi in hexanes (0.14 mL, 0.22 mmol) was added drop wise to the solution. The resulting mixture was stirred at -78 °C for five minutes and then quenched with excess CD_3OD (1 mL). The mixture was concentrated under reduced pressure and purified by flash chromatography (5% EA/Hex) to yield 27.5 mg (66%) of the title compound. R_f: 0.25 (5% EA/Hex). ^1H NMR (400 MHz): δ 1.29 (s, 9H), 1.97 (tdd, 2H, J= 6.5, 9.4, 6.4), 2.73 (AB dd, 2H), 4.00 (t, 2H, J= 6.5), 7.18-7.35 (m, 4H). ^{13}C NMR (100 MHz) : δ 26.4 (CH_3), 29.6 (CH_2), 32.4 (CH_2), 74.2 (CH_2), 80.1 (C), 125.8 (C), 128.2 (CH), 128.36 (CH), 128.42 (CH), 141.7 (C). HRMS (ESI): calcd for $C_{13}H_{19}DO_2$ $(M+Na)^+$: 232.1424; found: 232.1420.

Synthesis of Chroman (3,4-dihydro-2*H*-1-benzopyran) for GC-FID analysis:

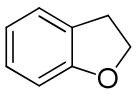


13

To a 0.5 M solution of 2-bromophenol (3.46 g, 20 mmol) in DMF was added potassium carbonate (5.5 g, 40 mmmol) followed by 1,3-dibromopropane (10 mL, 100 mmol). The reaction was stirred for 24 h and then quenched with sat. aq. NH_4Cl. The ether extract was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (5% EA/Hex) to yield 4.24 g (72%) of 2-bromophenyl 3-bromopropyl ether as a colorless oil. R_f: 0.45 (5% EA/Hex). ^1H NMR

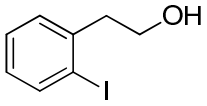
(400 MHz): δ 2.39 (quintet, 2H, J= 6.0), 3.71 (t, 2H, J= 6.0), 4.19 (t, 2H, J= 6.0), 6.87 (td, 1H, J= 7.6, 1.5), 6.95 (dd, 1H, J= 8.2, 1.4), 7.29 (m, 1H), 7.56 (dd, 1H, J= 7.9, 1.5). Spectra matched those previously reported for this molecule. (Bradsher, C. K.; J. Org. Chem. 1989, Vol. 46 (7), pp. 1384-1388)

To a 0.2 M solution of 2-bromophenyl 3-bromopropyl ether (588 mg, 2.0 mmol) in THF at -78 ^{o}C was added nBuLi (2.2 mmol, 1.4 mL of a 1.6 M solution in Hex) drop wise. The reation was allowed to warm to rt and after 1.5 h the reaction was quenched with sat. aq. NH_4Cl and extracted with ether. The resulting solution was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (2.5% EA/Hex) to yield chroman (3,4-dihydro-2*H*-1-benzopyran) 211 mg (79%) as a colorless oil. R_f: 0.3 (2.5 % EA/Hex). ^{1}H NMR (400 MHz): δ 2.04 (m, 2H), 2.83 (t, 2H, J= 6.6), 4.22 (app. triplet, 2H, J= 4.9) 6.80-6.89 (overlapping signals, 2H), 7.04-7.15 (overlapping signals, 2H). ^{13}C NMR (100 MHz): δ 22.4 (CH_2), 24.9 (CH_2), 66.4 (CH_2), 116.7 (CH), 120.1 (CH), 122.2 (C), 127.2 (CH), 129.8 (CH), 154.9 (C). Spectra matched those previously reported for this molecule. (Zhang, L., J. Org. Chem., 2009, Vol. 74 (7), pp. 2850-2853)



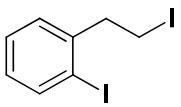
2,3-Dihydrobenzofuran (24)

The same protocol described for **13** was used for quantification of 2,3-dihydrobenzofurnan. A standard curve from commercial material (2,3-dihydrobenzofuran, purchased as a 99% grade from Sigma-Aldrich) was constructed using responses quantified for five different concentrations (mM, integration area): point 1 (0.33M, 7554161), point 2 (0.27M, 6183483), point 3 (0.22M, 5039547), point 4 (0.17M, 4013552), point 5 (0.12M, 2812031).



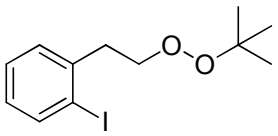
2-(2-Iodophenyl)ethanol (21)

2-(2-Iodophenyl)acetic acid (1.00 g, 3.8 mmol) was converted to the corresponding alcohol by the same procedure employed in compound **14** to yield 915 mg (97%) of the title compound as a colorless oil. R_f: 0.25 (20% EA/Hex). ^{1}H NMR (400 MHz): δ 3.05 (t, 2H, J= 6.8), 3.89 (t, 2H, J= 6.8), 6.95 (m, 1H), 7.25-7.35 (overlapping signals, 2H), 7.86 (dd, 1H, J= 7.8, 1.2). ^{13}C NMR (100 MHz): δ 43.7 (CH_2), 62.3 (CH_2), 100.0 (CH), 100.8 (C), 128.4 (CH), 130.4 (CH), 139.7 (CH), 141.1 (C). Spectra matched those previously reported for this molecule. (Minatti, A.; Org. Lett. 2008, V10(13), pg. 2721-272)



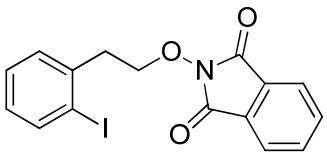
1-Iodo-2-(2-eodoethyl)benzene (22)

Alcohol **21** (898 mg, 3.62 mmol) was converted by the same procedure employed in compound **37** to yield 906 mg (70%) of the title compound as a light yellow oil. R_f: 0.95 (5% EA/Hex). ^{1}H NMR (400 MHz): δ 3.26-3.41(overlapping signals, 4H), 6.98 (m, 1H), 7.23-7.38 (overlapping signals, 2H), 7.85 (m, 1H). ^{13}C NMR (100 MHz): δ 3.3 (CH_2), 44.9 (CH_2), 99.9 (C), 128.5 (CH), 128.8 (CH), 129.8 (CH), 139.8 (CH), 143.3 (C). Spectra matched those previously reported for this molecule. (Minatti, A.; Org. Lett. 2008, V10(13), pg. 2721-2724)



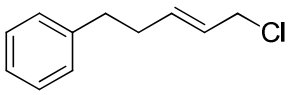
1-ethyl-2-iodobenzene *tert*-butyl peroxide (23)

Di-iodo compound **22** (107 mg, 0.3 mmol) was converted by the same procedure employed in compound **38** to yield 21.5 mg (22%) of the title compound as a light yellow oil. R_f: 0.80 (5% EA/Hex). ^{1}H NMR (400 MHz): δ 1.25 (s, 9H), 3.09 (t, 2H, J= 7.1), 4.15 (t, 2H, J= 7.1), 6.92 (m, 1H), 7.25-7.33 (overlapping signals, 2H), 7.83 (d, 1H, J= 7.7). ^{13}C NMR (100 MHz): δ 26.3 (CH_3), 39.3 (CH_2), 74.1 (CH_2), 80.4 (C), 100.6 (C), 128.2 (CH), 128.3 (CH), 130.3 (CH), 139.5 (CH), 141.2 (CH).



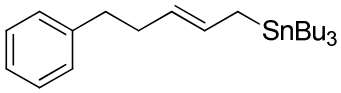
2-(2-Iodophenyl)-1-oxypthalimide ethane (25)

To a 0.1 M solution of alcohol (**21**) (496 mg, 2.0 mmol) in THF at 0 ^{o}C was added PPh_3 (629 mg, 2.4 mmol) and *N*-hydroxypthalimide (392 mg, 2.4 mmol) followed by the drop wise addition of diisopropyl azodicarboxylate (DIAD) (486 mg, 2.4 mmol). The resulting mixture was allowed to warm slowly to room temperature and stirred for 13 hours. The mixture was then diluted with Hex and pushed through a silica plug with 20% EA/Hex. The resulting solution was concentrated under reduced pressure and purified by column chromatography (10% EA/Hex) to yield 641 mg (82 %) of the title compound as a colorless oil. R_f: 0.3 (10% EA/Hex). ^{1}H NMR (400 MHz): δ 3.29 (t, 2H, J= 7.4), 4.43 (t, 2H, J= 7.4), 6.95 (td, 1H, J= 7.7. 1.7), 7.34 (td, 1H, J= 7.5, 1.3), 7.46 (dd, 1H, J= 7.6, 1.7), 7.75-7.81 (overlapping signals, 2H), 7.84-7.89 (overlapping signals, 3H). ^{13}C NMR (100 MHz): δ 39.5 (CH_2), 77.1 (CH_2), 100.6 (C), 123.6 (CH_2) 128.56 (CH_2), 128.61 (CH_2), 128.9 (CH_2), 130.3 (C), 134.5 (CH_2), 139.5 (C), 139.6 (CH), 163.6 (C).



(E)-(5-Chloropent-3-en-1-yl)benzene (29)

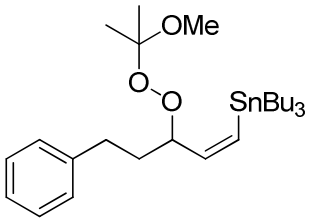
A 0.06 M solution of methylene chloride and commercially available 4-phenyl-1-butene (247 mg, 1.87 mmol) and allyl chloride (715 mg, 9.35 mmol) is stirred at 40 ^{o}C. A solution of Grubbs Catalyst 2nd Generation (1 mol %, 15.9 mg) was prepared in 5 mL of CH_2Cl_2. Half of this solution was added to initiate the reaction, followed by the remaining 2.5 mL one hour later. The mixture is allowed to react for 2 hours and then the reaction is then concentrated under reduced pressure and the residue purified by chromatography (100% Hex) to yield 172 mg (51%) of the title compound as a colorless oil. R_f: 0.4 (Hexanes). ^{1}H NMR (400 MHz): δ 2.24 (q, 2H, J= 7.7), 2.75 (t, 2H, J= 7.7), 4.06 (dd, 2H, J= 7.1, 0.8), 5.63-5.74 (m, 1H), 5.80-5.90 (m, 1H), 7.17-7.39 (m, 5H). ^{13}C NMR (100 MHz): δ 33.8 (CH_2), 35.3 (CH_2), 45.3 (CH_2), 125.9 (CH), 126.6 (CH), 128.38 (CH), 128.43 (CH), 135.0 (CH), 141.4 (C). Spectra matched those previously reported for this molecule. (Fuchter, M. J.; Org. Lett. 2008, vol. 10 (21), 4919-4922)



(E)-Tributyl(5-phenylpent-2-en-1-yl)stannane (30)

A 0.5 M solution of diisopropylamine (0.169 mL, 1.2 mmol) in THF was stirred at 0 ^{o}C. n-BuLi (1.6 M in Hex, 0.68 mL, 1.1 mmol) was added slowly dropwise and the resulting solution allowed to stir for 25 min at 0 ^{o}C. $HSnBu_3$ (0.291 g, 1 mmol) was then added neat and the resulting solution stirred for 30 min at 0 ^{o}C. The reaction mixture was then cooled to -78 ^{o}C and allylchloride **29** was added slowly as a solution in 0.6mL of THF.

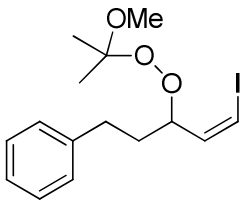
The reaction is allowed to slowly warm to room temperature. After 8 h the reaction was quenched with sat. aq. NH_4Cl and diluted with ether. The organic layer was separated and dried over Na_2SO_4. The resulting solution was then concentrated under reduced pressure and purified by chromatography (100% Hex) to yield 0.282 g (68%) of the title compound. R_f: 0.6 (Hex). ^{1}H NMR (400 MHz): δ 0.82-0.95 (m, 6H), 0.92 (t, 9H, J= 7.4), 1.25-1.38 (m, 6H), 1.44-1.55 (m, 6H), 1.71, (d, 2H, J= 8.5), 2.25-2.38 (m, 2H), 2.66 (t, 2H, J= 7.9), 5.23-5.35 (m, 1H), 5.53-5.68 (m, 1H), 7.16-7.25 (m, 3H), 7.26-7.34 (m, 2H). ^{13}C NMR (100 MHz): δ 9.1 (CH_3), 13.7 (CH_2), 14.2 (CH_2), 27.4 (CH_2), 29.2 (CH_2), 34.6 (CH_2), 36.7 (CH_2), 124.7 (CH), 125.6 (CH), 128.2 (CH), 128.4 (CH), 129.9 (CH), 142.4 (C). CAS #: 74940-41-3



(Z)-Tributyl(3-((2-methoxypropan-2-yl)peroxy)-5-phenylpent-1-en-1-yl)stannane (32)

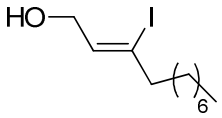
A 0.09 M solution of allyl stannane **30** (1.6 mmol, 0.700 g) and Rose Bangal (spatula tip) in CCl_4 (18 mL) was stirred vigorously under an atmosphere of oxygen and irradiated with a high intensity visible illuminator (Fiber-lite™ series 180, Dolan-Jenner Industries, Inc.) at a distance of 3 cm. After 5 h the solvent was removed under reduced atmosphere. The crude reaction mixture was partially purified by column chromatography (7.5%

EA/Hex), which yielded 155 mg of an impure product. This product obtained by chromatography dissolved in methylene chloride (5mL). Then 2-methoxypropene was added (40 mg, 0.57 mmol) followed by pyridinium p-toluene sulfonate (spatula tip) and the reaction stirred at room temperature for 1.5h. The reaction was then quenched with 5 mL of water, and the separated aqueous layer extracted with additional methylene chloride (10 mL X 3). The combined organic layers were dried with Na_2SO_4, concentrated under reduced pressure, and the residue purified by column chromatography (10% EA/Hex) to yield 155mg (18% yield over 2 steps) of the title compound as a colorless oil. R_f: 0.5 (10 EA/Hex). ^{1}H NMR (400 MHz): δ 0.86-0.96 (overlapping triplet with unresolved signal, 15H), 1.32 (app. sextet, 6H, J= 7.3), 1.41 (s, 3H), 1.45 (s, 3H), 1.51 (m, 6H), 1.77 (m, 1H), 2.03 (m, 1H), 2.75 (m, 2H), 3.34 (s, 3H), 4.23 (m, 1H), 6.11 (d, 1H, J= 12.9), 6.54 (dd, 1H, J= 12.9, 8.9), 7.17-7.25 (3H), 7.27-7.34 (2H). ^{13}C NMR (100 MHz): δ 10.4 (CH_3), 13.7 (CH_2), 22.8 (CH_3), 23.1 (CH_3), 27.3 (CH_2), 29.1 (CH_2), 31.8 (CH_2), 35.5 (CH_2), 49.2 (CH_3), 86.2 (CH), 104.3 (C), 125.9 (CH), 128.3 (CH), 128.4 (CH), 132.2 (CH), 141.9 (C), 148.3 (CH). HRMS (ESI): calcd for $C_{27}H_{48}O_3Sn$ $(M+Na)^+$: 563.2523; found: 563.2537. IR: 2954, 2923, 2871, 2359, 1455, 1376, 1366, 1260, 1208, 1183, 1152, 1071, 1030, 923, 847, 747, 697, 667, 590.



(Z)-(5-Iodo-3-((2-methoxypropan-2-yl)peroxy)pent-4-en-1-yl)benzene (33)

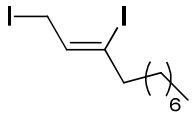
To a 0.05 M solution of stannane **32** (26 mg, 0.048 mmol) in THF was added *N*-iodosuccinamide (22 mg, 0.096 mmol). The reaction was stirred for 4 h at room temperature. The reaction mixture was then purified on a silica gel prep plate (10% EA/Hex) to yield 16.4 mg (90%) of the title compound. R_f: 0.45 (10% EA/Hex). ^{1}H NMR (400 MHz): δ 1.43 & 1.44 (unresolved singlets, 6H), 1.88 (m, 1H), 2.02 (m, 1H), 2.78 (m, 2H), 3.34 (s, 3H), 4.79 (td, 1H, J= 7.5, 5.4), 6.41 (t, 1H, J= 7.5), 6.47 (d, 1H, J= 7.7), 7.18-7.36 (5H). ^{13}C NMR (100 MHz) δ 22.7 (CH_3), 23.1 (CH_3), 31.4 (CH_2), 33.6 (CH_2), 49.5 (CH_3), 83.3 (CH), 85.3 (CH), 105.0 (C), 126.0 (CH), 128.4 (CH), 128.5 (CH), 141.2 (CH), 141.4 (C).



(Z)-3-Iodoundec-2-en-1-ol (36)

To a 0.26 M solution of alkynyl alcohol **34** (463 mg, 3.0 mmol) in THF at 0 ^{o}C was added Red-Al (4.8 mmol, 1.5 mL of 65% wt solution in toluene) drop wise. The reaction was allowed to warm to room temperature and stirred for 12 h. The reaction was then cooled to -78 ^{o}C and iodine (2.7 g, 11 mmol) was added as a solution in 0.5 mL of THF. The reaction was stirred at 0 ^{o}C for 1 h and then quenched with sat. aq. sodium potassium tartrate. The mixture was extracted with ether. The combined organic layers were washed sequentially with sat. aq. sodium potassium tartrate and aqueous sodium thiosulfate. The

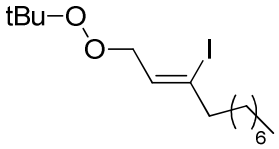
organic phase was then dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (10% EA/Hex) to yield 649 mg (77%) of the title compound. R_f: 0.6 (30% EA/Hex). ^{1}H NMR (400 MHz): δ 0.91 (t, 3H, J= 6.6), 1.22-1.38 (6H), 1.55 (quintet, 2H, J= 7.3), 2.51 (t, 2H, J= 7.3), 4.22 (d, 2H, J= 5.4), 5.85 (dt, 1H, J= 5.8, 1.1). ^{13}C NMR (100 MHz): δ 14.1 (CH_3), 22.6 (CH_2), 28.2 (CH_2), 29.0 (CH_2), 29.2 (CH_2), 31.7 (CH_2), 45.2 (CH_2), 67.3 (CH_2), 111.0 (C), 133.3 (CH). HRMS (ESI): calcd for $C_{11}H_{21}IO$ $(M+Na)^+$: 319.0535; found: 319.0532. IR: 3300, 2922, 2852, 1644, 1456, 1122, 1080, 1010, 721.



(Z)-1,3-Diiodoundec-2-ene (37)

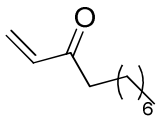
To a 0.2 M solution of iodo-allylalcohol **36** (1.41 g, 4.76 mmol) in CH_2Cl_2 at 0 ^{o}C was added PPh_3 (1.44 g, 5.5 mmol) and imidazole (443 mg, 6.5 mmol). Iodine (1.65 g, 6.5 mmol) in 5 mL of CH_2Cl_2 was added to the mixture in 3 portions over 10 min. After 1 h the reaction was diluted with hexanes and pushed through a silica plug. The resulting solution was then concentrated under reduced pressure and the residue purified by column chromatography (100% Hex) yielding 1.845 g (95%) of the title compound. R_f= 0.95 (100% Hex). ^{1}H NMR(400 MHz): δ 0.91 (t, 3H, J= 6.7), 1.22-1.34 (10H), 1.55 (quintet, 2H, J= 6.6), 2.53 (t, 2H, J= 7.2), 3.95 (d, 2H, J= 8.1), 5.83 (tt, 1H, J= 8.2, 1.1).

IR: 2952, 2921, 2851, 1625, 1456, 1424, 1376, 1289, 1142, 1142, 994, 840, 804, 721, 636.



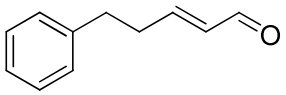
(Z)-3-Iodoundec-2-ene *tert*-butyl peroxide (38)

To 0.33M solution of tBuOOH (0.87 mL of a 5.5 M solution in decane, 4.8 mmol) in DMF at 0 ^{o}C was added CsOH monohydrate (806 mg, 4.8 mmol). The suspension was stirred for 30 min, and then diiodide **37** (1.62 g, 4.0 mmol) was added as a solution in 2.5 mL of DMF. The mixture was allowed to warm slowly to room temp. After 4.5 h the reaction was quenched with sat. aq. NH_4Cl and extracted with ether. The organic phase was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified via column chromatography (1% EA/Hex) to yield 374 mg (25%) of the title compound. R_f= 0.6 (5% EA/Hex). ^{1}H NMR (400 MHz): δ 0.91 (t, 3H, J= 6.8), 1.25-1.34 (singlet overlapping blob, 19H), 1.55 (quintet, 2H, J= 6.9), 2.52 (t, 2H, J= 7.0), 4.52 (d, 2H, J= 5.7), 5.87 (tt, 1H, J= 5.7, 1.1). IR: 2924, 2854, 1644, 1458, 1362, 1242, 1195, 1127, 1082, 1042, 1016, 880, 755, 721, 609.



Undec-1-en-3-one (39)

To a -78 ^{o}C 0.05M solution of iodo peroxide **38** (37 mg, 0.1 mmol) in THF was added nBuLi dropwise as a 1.6 M solution in hexane (0.2 mmol, 0.125 mL). The reaction was stirred for 30 min and then quenched with sat. aq. NH_4Cl and allowed to warm to room temperature. The mixture was extracted with ether, and the organic layer dried with Na_2SO_4 and concentrated under reduced pressure. Attempts to purify the title compound failed. In ^{1}H NMR analysis of the crude residue signals for vinyl protons as well as protons beta to the carbonyl.



(E)-5-Phenylpent-2-enal (40)

To a -78^{o}C solution of stannyl peroxide **32** (17.3 mg, 0.032 mmol) in THF 0.06 M was added nBuLi dropwise as a 1.6 M solution in hexane (4 drops, ~20 μL, ~0.032 mmol). The reaction was kept at -78 ^{o}C and an additional 1 equivalent of nBuLi was added every 10 min until the starting material was consumed via TLC (total of 4 equivalents of nBuLi added). The reaction was then quenched with sat. aq. NH_4Cl and allowed to warm to room temperature. The mixture was extracted with ether. The ether extract was dried with Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (10% EA/Hex) to yield 0.6 mg (~10%) of the title compound. R_f: 0.2 (10% EA/Hex). ^{1}H NMR (400 MHz): δ 2.70 (m, 2H), 2.86 (t, 2H, J= 7.8), 6.16 (ddt, 1H,

J= 15.7, 7.8, 1.5), 6.88 (dt, 1H, J= 15.7, 6.7), 7.19-7.28 (3H), 7.30-7.37 (2H). ^{1}H NMR data matched those previously reported for this molecule. (Palais, L., Babel, L., Quintard, A., Belot, S., Alexakis, A., Org. Lett., 2010, 12(9) pp. 1988-1991)