JOC Article

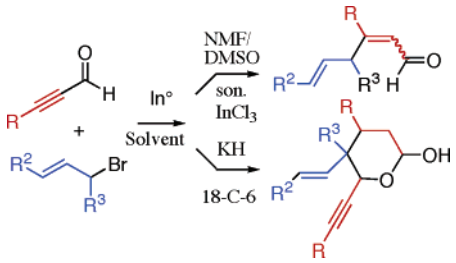
Control of Skeletal Connectivity in Indium Promoted Reactions: 1,2-Additions and Cope Rearrangements En Route to Lactol Formation

Thomas Mitzel,* Joe Wzorek, Annie Troutman, and Kristen Allegue

Department of Chemistry, Trinity College, 300 Summit Street, Hartford, Connecticut 06106

thomas.mitzel@trincoll.edu

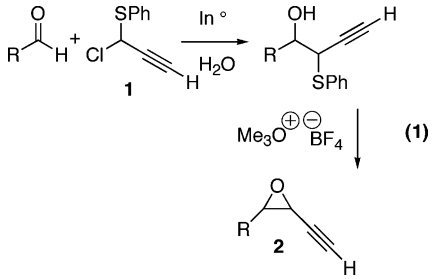
Received January 4, 2007



Indium promoted coupling reactions between propargyl aldehydes (**3**) and allyl halides under aqueous and organic conditions are reported. Coupling reactions under aqueous conditions occur via 1,2-addition with excellent yields to afford 4-hydroxy-1-ene-5-ynes (**8**). Coupling reactions under organic conditions also add in a 1,2-fashion, but the initial products can be induced to undergo oxy-Cope rearrangements giving 2,5-hexadienals (**9**). Oxy-Cope rearrangement of **8** followed by a secondary addition step under highly basic conditions leads to lactol formation (**10**) in good to excellent yields. This paper reveals the versatility and control of product formation which may be attained when working with propargyl aldehyde (**3**) and allyl halide systems under indium promoted coupling conditions.

Introduction

Previous work in our laboratory has focused on stereocontrolled coupling reactions between α-chloropropargyl phenyl sulfide (**1**) and aldehyde partners.[1] This work culminated in stereocontrolled formation of epoxyalkyne structures (**2**) which find wide use as synthetic templates in natural product syntheses (eq 1).[2] A natural extension of this chemistry was to utilize a



propargyl aldehyde (**3**)[3a] as the electrophilic component, forming a β-hydroxy phenyl sulfide structure (**4**), which could then be converted to either an enediyne (**5**) or an epoxydiyne (**6**) (eq 2). Both enediyne and epoxydiyne functional groups are present in natural products shown to have anticarcinogenic properties.[4] This system was intriguing due to the short synthetic route, good stereocontrol of the coupling step with indium organometallics to aldehydes as shown in previous studies,[1] and benign conditions under which indium promoted C−C bond forming reactions of this type are conducted.

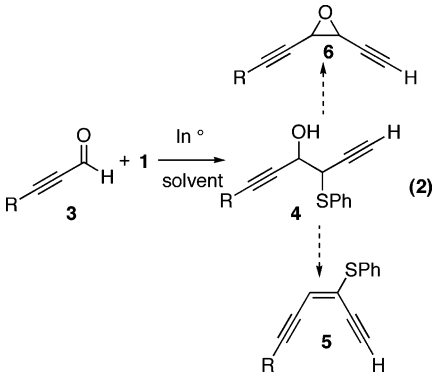
(1) (a) Engstrom, G.; Morelli, M.; Palomo, C.; Mitzel, T. *Tetrahedron Lett.* **1999**, *40*, 5967. (b) Palomo, C.; Jendza, K.; Mitzel, T. M. *J. Org. Chem.* **2002**, *67*, 136.

(2) (a) Odedra, A.; Wu, C.-J.; Madhushaw, R. J.; Wang, S.-L.; Liu, R.-S. *J. Am. Chem. Soc.* **2003**, *125*, 9610. (b) Lo, C.-Y.; Guo, H.; Lian, J.-J.; Shen, F.-M.; Liu, R.-S. *J. Org. Chem.* **2002**, *67*, 3930. (c) Kanger, T.; Piret, J.; Müürisep, A. M.; Pek, T.; Lopp, M. *Tetrahedron: Asymmetry* **1998**, *9*, 2499. (d) Bernard, N.; Chemla, F.; Normant, J. F. *Tetrahedron Lett.* **1998**, *39*, 6715. (e) Aurrecoechea, J. M.; Alonso, E.; Solay, M. *Tetrahedron* **1998**, *54*, 3833. (f) Piotti, M. E.; Alper, H. *J. Org. Chem.* **1997**, *62*, 8484. (g) Wu, S. H.; Huang, B. Z.; Gao, X. *Synth. Commun.* **1990**, *20*, 1279. (h) Bohlmann, F.; Burkhardt, T.; Zdero, C. *Naturally Occurring Acetylenes*; Academic Press: New York, 1973.

(3) Examples of formation of propargyl aldehydes: (a) Journet, M.; Cai, D.; DiMichele, L. M.; Larsen, R. D. *Tetrahedron Lett.* **1998**, *39*, 6427. (b) Jackson, M. M.; Leverett, C.; Toczko, J. F.; Roberts, J. C. *J. Org. Chem.* **2002**, *67*, 5032. (c) Dixon, D. J.; Ley, S. V.; Tate, E. W. *Synlett* **1998**, 1093. (d) Trost, B. M.; Schmidt, T. *J. Am. Chem. Soc.* **1988**, *110*, 2301. (e) Molander, G. A.; McWilliams, J. C.; Noll, B. C. *J. Am. Chem. Soc.* **1997**, *119*, 1265. (f) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815.

10.1021/jo070020k CCC: $37.00
Published on Web 03/10/2007

Study of the above system, as will be discussed, led to detection of an interesting side product that appeared to be formed by either a Michael addition or a 1,2-addition followed by a Cope rearrangement. Formation of this side product was found to be solvent dependent, raising interesting theoretical and regiocontrol questions pertaining to indium promoted couplings involving systems containing both conjugated electrophilic and nucleophilic species. Recent work by Loh et al.,[5] Li et al.,[6] and Chan et al.,[7] which has focused on coupling of conjugated indium species with carbonyl moieties and the effects of solvent conditions upon regiocontrol, has revealed an exciting area of chemistry in which good work has been accomplished, but many questions still remain. This paper focuses on the study of the addition of allylic indium organometallic species to propargyl aldehyde partners and the effects of solvent and reaction conditions on final product formation, with emphasis on construction of six-membered ring lactols in good yields.



Results and Discussion

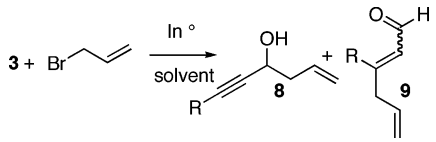
Early Studies. Studies in this area began with an examination of indium coupling reactions of propargyl aldehydes (**3**) with α-chloropropargyl sulfide (**1**). Product formation was shown to be solvent dependent, with clean 1,2-addition observed under aqueous conditions but mixtures of isomeric products formed under organic conditions (Table 1). The percent recovery of product mixture, while excellent in water, was quite low in organic solvents, rendering isolation and full characterization of the side product within this particular system difficult. A plausible structure for the isomeric byproduct is **7**. The difference witnessed in regioselectivity, which appeared to be linked to solvent conditions, was intriguing and warranted further investigation. First, however, it was necessary to determine beginning conditions that could maximize yields of product in nonaqueous systems.

Model System/Mechanistic Hypothesis. As a result of difficulties noted with isolation and characterization of mixtures reported in Table 1, the system was simplified, replacing **1** with a structurally more simplistic allyl bromide as the source of the nucleophilic species. Conditions mentioned in Table 1 were replicated with the new system, yielding results shown in Table 2.

TABLE 1. Ratio of 1,2-Addition Product (4) vs Plausible Product of Side Reaction (7)

entry	R	H_2O	3:1 H_2O/DMF	DMF (ratio of **4**/**7**)
1	TMS	only 1,2-	only 1,2-	3:1
2	*n*-butyl	only 1,2-	only 1,2-	1.5:1
3	phenyl	only 1,2-	only 1,2-	1:4
4	$TBSO(CH_2)_3$	only 1,2-	only 1,2-	2:1

TABLE 2. Coupling of 3 and Allyl Bromide under Aqueous and Organic Conditions



entry	R	solvent	ratio: **8**/**9**	recovery (%)
1	TMS	H_2O	only 1,2	55
2		DMF	7:1	57
3		THF	1:3	8
4	*n*-butyl	H_2O	only 1,2	87
5		DMF	5:1	85
6		THF	1:3	7
7	phenyl	H_2O	only 1,2	90
8		DMF	6:1	87
9		THF	1:4	7
10	$TBSO(CH_2)_3$	H_2O	only 1,2	53
11		DMF	10:1	55
12		THF	1:2	9

Use of organic solvent conditions resulted in a mixture of **8** and **9** as shown. The percent recovery of products was good in DMF but very low in THF. Indium promoted coupling reactions have historically been shown to proceed more quickly and in higher percent yields in more polar solvents, so this finding was not too surprising.[1,8] Using water as a solvent, only **8** was formed. On the basis of this outcome, it was theorized that **9** formed via an oxy-Cope rearrangement,[9] following the pathway proposed in Scheme 1. The first step along this mechanistic pathway is a 1,2-addition, forming an oxy-intermediate chelated to the indium complex.[9c] Under aqueous conditions, this

(4) (a) Galm, U.; Hager, M. H.; Van Lanen, S. G.; Ju, J.; Thorson, J. S.; Shen, B. *Chem. Rev.* **2005**, *105*, 739. (b) Basak, A.; Mandal, S.; Bag, S. S. *Chem. Rev.* **2003**, *103*, 4077. (c) Konig, B.; Pitsch, W.; Klein, M.; Vasold, R.; Prall, M.; Schreiner, P. R. *J. Org. Chem.* **2001**, *66*, 1742. (d) Shair, M. D.; Yoon, T. Y.; Mosny, K. K.; Chou, T. C.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1996**, *118*, 9509. (e) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25.

(5) Lin, M. J.; Loh, T. P. *J. Am. Chem. Soc.* **2003**, *125*, 13042.

(6) Yi, X. H.; Meng, Y.; Hua, X. G.; Li, C. J. *J. Org. Chem.* **1998**, *63*, 7472.

(7) (a) Isaac, M. B.; Chan, T. H. *Chem. Commun*. **1995**, 1003. (b) Chan, T. H.; Yang, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3228.

(8) For reviews and examples: (a) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095. (b) Araki, S.; Hirashita, T. In *Main Group Metals in Organic Synthesis*; Yamamoto, H., Oshima, K., Eds.; Wiley-VCH: Weinheim, Germany, 2004; Vol. 1, pp 323−386. (c) Paquette, L. A. In *Green Chemistry: Frontiers in Benign Chemical Synthesis and Processing*; Anastas, P., Williamson, T., Eds.; Oxford University Press: New York, 1998. (d) Li, C. J.; Chan, T. H. *Organic Reactions in Aqueous Media*; John Wiley & Sons: New York, 1997. (e) Li, C. J.; Chan, T. H. *Tetrahedron* **1999**, *55*, 11149. (f) Paquette, L. A.; Mitzel, T. M. *J. Am. Chem. Soc.* **1996**, *118*, 1931.

(9) For reviews and examples: (a) Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. *Organic Chemistry*; Oxford University Press: New York, 2001; pp 947−951. (b) Gagosz, F. *Org. Lett.* **2005**, *7*, 4129. (c) White, B. H.; Snapper, M. L. *J. Am. Chem. Soc.* **2003**, *135*, 14901−14904. (d) Santora, V. J.; Moore, H. W. *J. Org. Chem*. **1996**, *61*, 7976. (e) Viola, A.; MacMillan, J. H. *J. Am. Chem. Soc.* **1970**, *92*, 2404.

SCHEME 1. Hypothesized Oxy-Cope Rearrangement

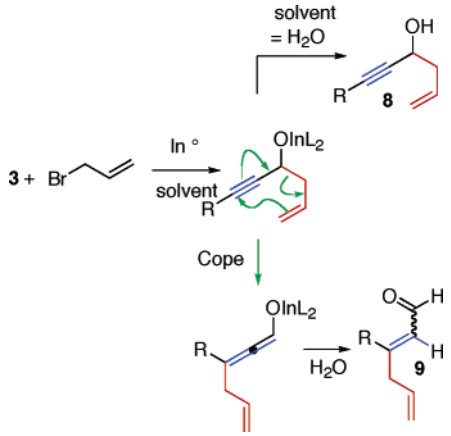
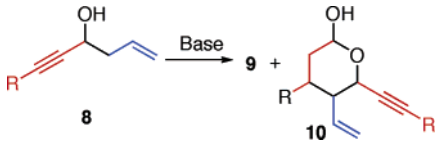


TABLE 3. Conditions To Induce Cope Rearrangement



entry	base	conditions	product mixture (recovery %) 8	9	10
1	Amberlite resin	stirring	100	0	0
2	Amberlite resin	column	100	0	0
3	$KN(TMS)_2$	−78 °C, THF	100	0	0
4	$KN(TMS)_2$	−78 °C to rt, THF	decomposition[a]		
5	*n*-BuLi	−78 °C, THF	85	15	0
6	*n*-BuLi	−78 °C to rt, THF	35	65	0
7	NaH	−78 °C to rt, THF	100	0	0
8	KH	−78 °C, THF	100	0	0
9	KH	−78 °C to rt, THF	decomposition[a]		
10	KH	−78 °C to 40 °C, THF	0	0	100

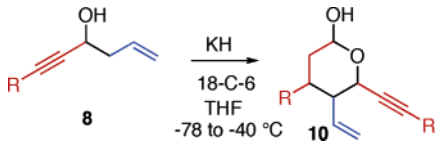
[a] Entries 4 and 9 resulted mostly in decomposition of starting material.

intermediate quickly picks up a proton to give **8**. Under organic conditions, where no proton source is present, the oxy-indium intermediate is long-lived, and the unprotonated oxygen is much more likely to promote an oxy-Cope rearrangement to form an allenol intermediate. The formation of an allenol intermediate was shown to occur with hexen-1-yn-3-ol thermolytically in 1970, and it seems reasonable that this intermediate is forming under our conditions as well.[9c] After rearrangement occurs, the ensuing allenyl intermediate is protonated and tautomerizes upon workup to give **9** as the final structure. From Table 2, it is seen that the Cope rearrangement, if this is indeed the pathway followed, does not occur efficiently, so it was necessary to determine conditions that would maximize the potential of rearrangement, increasing the percent formation of **9**.

Cope Rearrangement and Lactol Formation. Since it was possible to form **8** in high yield under aqueous conditions, it was initially decided to isolate this product and promote the oxy-Cope rearrangement in a second, separate step. Several reagents were tested for this purpose as shown in Table 3.

Amberlite IRA-900 ion-exchange resin with a benzyltrialkylammonium functionality was utilized to determine if conversion could occur under mild conditions. Alcohol (**8**) was both stirred with Amberlite resin and "washed" down the resin in column chromatography fashion using hexanes as the eluent. In neither case did rearrangement occur, and starting material was isolated pure. Use of potassium bis(TMS) amide[10a] resulted in decomposition of the starting material at room temperature. At −78 °C, no reaction occurred with this reagent. Mixing **8** with *n*-BuLi gave a small amount of **9** at both −78 °C and room temperature; however, much decomposition was noted under both conditions. Sodium hydride[10b] resulted in no rearrangement at any temperature. Potassium hydride[10c] proved to be best for inducing oxy-Cope rearrangement of **8**, with rearrangement occurring at approximately −40 °C in a THF mixture of **8** and KH in the presence of 18-crown-6. TLC and MS data revealed disappearance of all starting material and formation of a single product. To our surprise, the data did not match a structure consistent with **9** but rather matched that of **10**, a lactol.[11,12] Lactols create much interest in carbohydrate chemistry[11] and as organic templates,[12] so we were quite motivated to elucidate the mechanism of formation for the lactol product and how it related to an oxy-Cope rearrangement. To determine the efficiency of this transformation, a series of propargyl homoallylic alcohols (**8**) was exposed to KH in the presence of 18-crown-6. In each case, the starting material, dissolved in THF, was cooled to−78 °C at which time KH and 18-crown-6 were added. After stirring at −78 °C for 30 min, the reaction mixture was raised to −40 °C where it was kept until TLC revealed the disappearance of the starting alcohol and appearance of product. The reactions were very clean and are summarized in Table 4. Use of 18-crown-6 was necessary to promote the reaction. Mixing of **8** with KH in the absence of 18-crown-6 led to decomposition of the starting material with no discernible product formed.

TABLE 4. Lactol Formation Using 3 Containing Varying R Groups



entry	R	recovery (%)
1	$H_3C(H_2C)_4$−	93
2	$H_3C(H_2C)_3$−	89
3	Ph	23
4	TMS[a]	25

[a] When R = TMS in the starting alcohol, R = H in the final product.

Although results from Table 4 do not present a product arising from a straightforward Cope rearrangement, closer scrutiny of the system reveals this is indeed what occurs. Previous work[13] with anionic oxy-Cope rearrangements has noted a fairly common side reaction involving fragmentation of unsaturated groups at the β-position to an alcohol moiety. For our system,

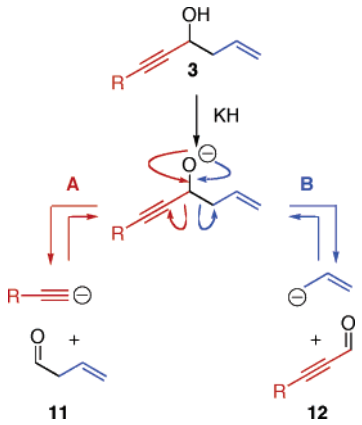
(10) Representative examples: (a) Tsui, H.-C.; Paquette, L. A. *J. Org. Chem.* **1998**, *63*, 9968. (b) Evans, D. A.; Baillargeon, D. J.; Nelson, J. V. *J. Am. Chem. Soc.* **1978**, *100*, 2242. (c) Wei, S.-Y. Tomooka, K.; Nakai, T. *J. Org. Chem.* **1991**, *56*, 5973.

(11) (a) Cuerrier, D.; Moldoveanu, T.; Inoue, J.; Davies, P. L.; Campbell, R. L. *Biochemistry* **2006**, *45*, 7446. (b) Yu, X.-M.; Han, H.; Blagg, B. S. J. *J. Org. Chem.* **2005**, *70*, 5599. (c) Bates, R. B.; Haber, W. A.; Setzer, W. N.; Stessman, C. C. *J. Nat. Prod.* **1999**, *62*, 340.

(12) (a) Vu, C. C.; Peterson, L. A. *Chem. Res. Toxicol.* **2005**, *18*, 1012. (b) Pansare, S. V.; Jain, R. P. *Org. Lett.* **2000**, *2*, 175. (c) Buckley, N.; Oppenheimer, N. J. *J. Org. Chem.* **1996**, *61*, 8048.

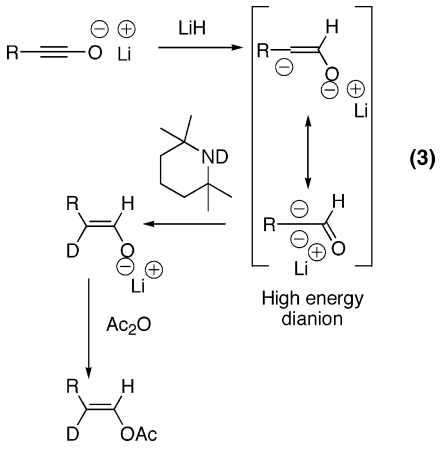
(13) (a) Wilson, S. *Org. React.* **1993**, *43*, 93. (b) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205.

SCHEME 2. Fragmentation Pathway for Anionic Oxy-Cope



the fragments shown in Scheme 2 could arise from this type of cleavage. This step is reversible, and re-formation of the two fragments is possible, especially under strongly basic conditions. When R = phenyl, the product mixture contains a large amount of **12**, indicating that bond cleavage occurs quickly with little recombination of the fragments and that rearrangement is slower than cleavage. We have not seen evidence for **11** or products that could arise from the alkynyl anion in our product mixtures. MS data associated with **12** are detected in all systems. When R = alkyl, **12** is not witnessed in our final product mixture, and product recoveries are as high as 93% (Table 4, entry 1). It is surmised that **12** is integrated into the final lactol structure by reaction with the anion of **9** as shown in Scheme 3. Initial oxy-Cope rearrangement gives an anion intermediate (**A**). Under the highly basic conditions, KH may remove a proton from the acidic doubly allylic proton position in structure **A** of Scheme 3.

A dianionic species such as one that would form from **A** is feasible and has literature precedence.[14] The dianion formed by deprotonation of **A** reacts with **12**, giving allenic anion (**B**). At this stage, reduction of the sp-hybridized atom in the allene occurs by interaction with KH. Although this step is a bit unconventional, Kowalski et al.[15] have shown a similar reduction of sp-centers with an alkali metal hydride (eq 3[15b]), and other

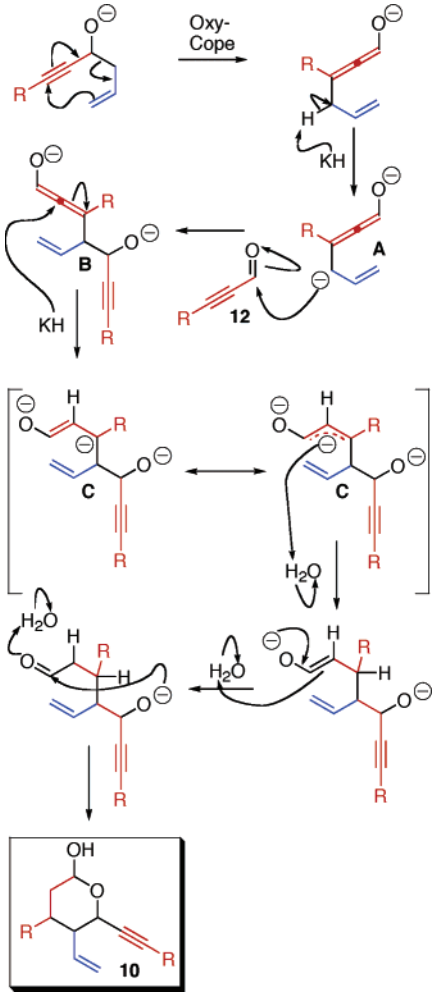


(3)

work has shown the propensity for KH and other metal hydrides

(14) Dimmel, D. R.; Charpure, S. B. *J. Am. Chem. Soc.* **1971**, *93*, 3991.
(15) (a) Kowalski, C. J.; Haque, S. *J. Am. Chem. Soc.* **1986**, *108*, 1325. (b) Kowalski, C. J.; Lal, G. S. *J. Am. Chem. Soc.* **1986**, *108*, 5356.

SCHEME 3. Lactol Formation by Reaction Cope Dianion with 12



to act as reducing agents.[16] The dianionic intermediate proposed in Kowalski's work reveals the viability of forming these multicharged species under highly basic conditions.[15a,b] Finally, quenching of the anionic intermediate (**C**) leads to **10** as shown in Scheme 3.[17] Formation of this anionic species would argue toward highly basic conditions being necessary to drive this reaction in THF, and indeed an increase in the amount of KH (up to 4 equiv) accelerates the reaction and raises the yield of lactol product. To provide further evidence for this pathway, substituted allylic systems (**13**, **14**) were used in the addition/rearrangement reaction. Crotyl bromide was used to form **13** while 3-chloro-1-butene was used to form **14**. As shown in Scheme 4, each of these systems forms a lactol structure which would be predicted following the mechanistic pathway in Scheme 3. The yield for **15** is low, which is believed to be due to the second allylic position present in the intermediate shown in Figure 1. Deprotonation may occur from the second allylic site, giving rise to other products and lowering the overall

(16) (a) Pi, R.; Friedl, T.; Schleyer, P. v. R.; Klusener, P.; Brandsma, L. *J. Org. Chem.* **1987**, *52*, 4299. (b) Zippi, E. M. *Synth. Commun.* **1994**, *24*, 2515. (c) Ohkuma, T.; Shohei, H.; Noyori, R. *J. Org. Chem.* **1994**, *59*, 217. (d) Zhang, W.; Liao, S.; Xu, Y. Zhang, Y. *Synth. Commun.* **1997**, *27*, 3977.
(17) For an NMR comparison of a lactol containing similar structural qualities: Barlow, A. J.; Compton, B. J.; Weavers, R. T. *J. Org. Chem.* **2005**, *70*, 2470.

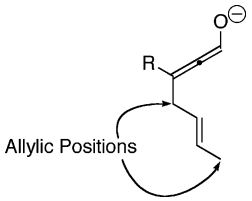
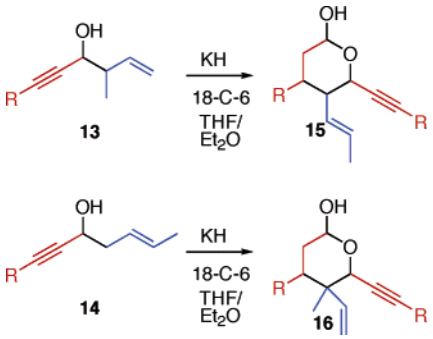


FIGURE 1. Allylic sites available for deprotonation under anionic rearrangement conditions for **13**.

SCHEME 4. Use of Substituted Allylic Systems

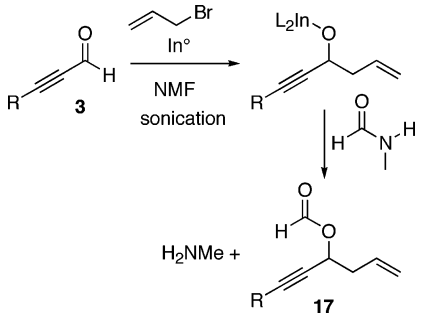


product yield. When **13** was exposed to KH/18-crown-6 in THF as the sole solvent, the solution quickly turned black, and no product was isolated from the mixture. Use of Et_2O as a cosolvent (30%), however, gave rise to the formation of lactol, albeit in a low yield (9.5%). Use of **14** also required Et_2O as a cosolvent during the reaction and resulted in formation of **16** in 40% yield. In each case, the mechanistic pathway proposed in Scheme 3 is confirmed, giving strong evidence for the oxy-Cope rearrangement. Entry 4 from Table 4 is interesting in that the final product is lacking the TMS groups originally present in the starting material. These groups appear to be cleaved during workup of the product mixture. The highly basic conditions present during this reaction system promote formation of hydroxy anions during quenching and workup, creating conditions conducive to cleavage of the TMS groups.[18]

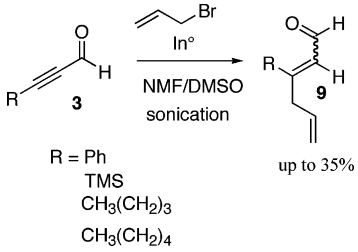
One-Pot Coupling/Cope Rearrangement. With the mechanism of product formation clarified and control of the lactol products discovered, the final goal was to promote both a coupling reaction and Cope rearrangement in a one-pot sequence. As Table 2 shows, some Cope product was formed in reactions conducted in DMF and THF. It is assumed the oxy-organometallic complex formed in the coupling step may rearrange if oxygen remains unprotonated. Yields of conversion in DMF and THF at room temperature were low, so conditions that may help raise overall yields and conversion rates were sought. Reactions outlined in Table 1 were repeated in DMF and THF with heating. In both cases, yields were not raised and decomposition of the mixture actually increased in DMF around 50 °C.

Sonication of the reaction mixtures was next attempted. Percent formation of **9** increased slightly in DMF but never above 11%. Initial coupling to form **7** increased significantly in THF with sonication, with yields over 80% realized; however, an increase of Cope product was not witnessed under these conditions.

SCHEME 5. Formation of Ester Product



SCHEME 6. Formation of Cope Product via Cascade Conditions



We next turned to a seldom used solvent, *N*-methylformamide (NMF).[19] The choice of NMF was determined by our need for a very polar, organic solvent. NMF has a dielectric constant of 186.9,[19a] significantly greater than that of water at 78.37.[19b] It was our hope that NMF would be polar enough to allow the oxy-indium complexed intermediate to be sufficiently long-lived to promote Cope rearrangement. As before, the coupling reaction of **3** and allyl bromide was conducted at room temperature with stirring. Although **8** was formed in good yield (80−95%), no Cope product was produced under these conditions. Heating caused an increase in the reaction rate en route to **8** but, again, no Cope product. Cooling the NMF system to 0 °C provided interesting results, as some of the systems revealed an increased rate of coupling at this temperature compared to room temperature, but again, no Cope product was isolated. It is possible the oxy-anion intermediate is hydrogen bonding with the amide proton of NMF, raising the energy for an oxy-Cope reaction to occur. Upon workup of this reaction with water, **8** was isolated as the product.

The system was sonicated next. It was hoped that the extra energy offered by sonication would promote Cope rearrangement. There was indeed a minor, secondary reaction, resulting from **8**; however, it was determined that the oxy-indium complex was reacting with NMF to form ester **17** as shown in Scheme 5. Various Lewis acids were then tested, with the thought that a Lewis acid may chelate with the oxygen atom, reducing interaction of the oxygen with NMF, but **17** was formed under Lewis acid conditions as well. Dimethylsulfoxide (DMSO) was introduced as a cosolvent (DMSO/NMF (1:1)) in the presence of a Lewis acid, and this change solved our problem to an extent (see Scheme 6). Under cosolvent conditions, **9** was isolated in yields up to 35%. Overall recovery of the product mixture was approximately 45% with **17** and **8** making up the additional 10%. To determine whether the initial step of this reaction was a Michael addition or a 1,2-addition followed by a Cope rearrangement, aliquot workups were performed during the course of the study. After approximately 30 min, formation of the 1,2-addition product was witnessed in all systems. After approximately 2−4 h, **8** was the sole species in the reaction

(18) Abad, A.; Agullo, C.; Cunat, A. C.; Perni, R. H. *J. Org. Chem.* **1999**, *64*, 1741.
(19) (a) Rohdewald, P.; Moldner, M. *J. Phys. Chem.* **1973**, *77*, 373. (b) Vidulich, G. A.; Kay, R. L. *J. Phys. Chem.* **1962**, *66*, 383.

mixture, signifying 1,2-addition of the organometallic to the aldehyde. After 24 h of reaction, traces of **17** and **9** began to build in the mixture until it reached a peak after 72−84 h at which time the reaction was stopped. At no time were fragmentation products (Scheme 2) isolated in the mixtures which signifies coupling initially occurs by 1,2-addition which is then followed by a Cope rearrangement to give **9**. Although yields of the Cope product are modest, this is a nice cascade, one-pot reaction sequence which can be controlled with only slight solvent modifications. DMSO as the sole solvent was not effective in promoting formation of **9**. Use of DMSO as the sole solvent yielded mainly **8** with only traces of **9** as witnessed by GC−MS. In the absence of sonication, only **8** is isolated in excellent yields. If the reaction mixture is sonicated, **9** is formed in modest yields beginning from uncoupled aldehyde **3** and an allyl halide.

Conclusion

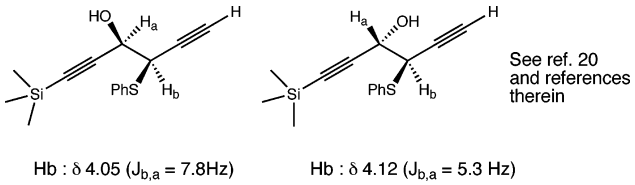
Indium promoted coupling of propargyl aldehydes (**3**) with allyl halides results in the formation of propargyl alcohols (**8**) under aqueous and organic conditions in good to excellent yields. Use of the NMF/DMSO solvent mixture under sonication affords a Cope rearrangement product (**9**) in modest yields, revealing good regiocontrol in bond formation of these systems. Exposure of **8** to KH−18-crown-6 in THF or THF−Et_2O solutions at low temperatures results in formation of lactol compounds (**10**) in modest to excellent yields affording entry to synthetic templates for use in natural product syntheses. These three sets of reaction conditions offer nice versatility in bond-forming reactions leading to controlled formation of very different products beginning from an identical starting system by altering reaction conditions slightly in each case.

Experimental Section

General Experimental Procedures. Tetrahydrofuran was purified by distillation under an argon atmosphere over sodium and benzophenone prior to use. Dimethylformamide and CCl_4 were purified by distillation over CaH_2 prior to use. All other solvents were used as purchased. 18-Crown-6 was purified before use. All other reagents were used as purchased. Radial chromatography was performed using a Chromatotron.

I. Coupling Procedures for Propargyl Aldehyde (3) with α-Chloropropargyl Phenyl Sulfide (1). I.a. General Procedure Using Water as Solvent. A magnetically stirred solution of aldehyde (**3**) (2.2 mmol) in deionized water (22 mL) was treated with α-chloropropargyl phenyl sulfide (702 mg, 3.0 mmol) and indium powder (252 mg, 2.2 mmol). The solution was allowed to proceed at room temperature until no **3** was seen (TLC analysis). Dichloromethane was added, and stirring was maintained for 30 min. The layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were dried over $MgSO_4$ and evaporated to leave a dark yellow to brown oil. Purification was accomplished by flash chromatography or radial chromatography on silica gel (hexanes−ethyl acetate) to give a mixture of hydroxy sulfides[20] as a light yellow oil. No Cope product was witnessed under aqueous conditions.

I.a.1. Use of 3-Trimethylsilypropynal (R = TMS) with α-Chloropropargyl Phenyl Sulfide (1). Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (35:1 hexanes−ethyl acetate) to give a mixture of diastereomeric hydroxy sulfides. Yield = 418 mg (1.54 mmol) = 70%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.24 (s, 9H), 1.79 (d, J = 1.7 Hz, 0.25H), 1.84 (d, J = 1.6 Hz, 0.75H), 4.15 (dd, J = 1.7, 7.8 Hz, 0.25H), 4.23 (dd, J = 1.6, 5.3 Hz, 0.75H), 4.69 (d, J = 7.8 Hz, 0.25H), 4.80 (d, J = 5.3 Hz, 0.75H), 7.1−7.4 (m, 5H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.28 (44.1, 44.4), (66.5, 68.1), (67.5, 67.9), (74.1, 75.0), (83.2, 84.3), (86.4, 86.9), 125.0, 125.3, 126.5 (2), 127.3, 136.1; MS m/z (M^+) calcd 274.0848, obsd 274.0819. Anal. Calcd for $C_{15}H_{18}OSSi$: C, 65.64; H, 6.61. Found: C, 65.17; H, 6.55.



I.a.2. Use of 2-Heptynal (R = *n*-C_4H_9) with α-Chloropropargyl Phenyl Sulfide (1). Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (40:1 hexanes−ethyl acetate) to give a mixture of diastereomeric hydroxy sulfides. Yield = 471 mg (1.76 mmol) = 83%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.9−1.5 (m, 7H), 1.82 (d, J = 1.7 Hz, 0.2H), 1.87 (d, J = 1.6 Hz, 0.8H), 2.13 (t, J = 6.5 Hz, 2H), 4.09 (m, 1H), 4.86 (m, 1H), 7.1−7.3 (m, 5H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.5, 18.2, 21.3, 34.2, (41.5, 42.9), (65.0, 66.1), 71.3, 78.5, 80.2, 84.7, 125.4, 126.1, 126.3, 127.6, 128.0, 136.4; MS m/z (M^+) calcd 258.1078, obsd 258.0998. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.38; H, 7.02. Found: C, 74.61; H, 6.99.

I.a.3. Use of 3-Phenylpropynal (R = Phenyl) with α-Chloropropargyl Phenyl Sulfide (1). Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (35:1 hexanes−ethyl acetate) to give a mixture of diastereomeric hydroxy sulfides. Yield = 489 mg (1.78 mmol) = 80%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.83 (d, J = 1.8 Hz, 0.2H), 1.94 (d, J = 1.8 Hz, 0.8H), 3.95 (dd, J = 1.8, 8.1 Hz, 0.2H), 4.10 (dd, J = 1,8, 4.7 Hz, 0.8H), 4.95 (d, J = 8.1 Hz, 0.2H), 5.11 (d, J = 4.7 Hz, 0.8H), 7.2−7.7 (m, 10H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ (43.8, 44.1), (65.8, 66.0), 68.0, 81.3, 87.2, 93.6, 121.7, 125.8 (2), 127.3 (3), 128.1, 128.3(2), 129.3, 129.5, 136.1; MS m/z (M^+) calcd 278.0765, obsd 277.9986. Anal. Calcd for $C_{18}H_{14}OS$: C, 77.66; H, 5.07. Found: C, 77.28; H, 5.18.

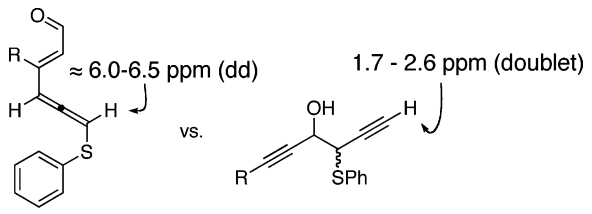
I.a.4. Use of 6-(*tert*-Butyldimethylsiloxy)-2-hexynal (R = $(CH_2)_3$−OTBS) with α-Chloropropargyl Phenyl Sulfide (1). Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (35:1 hexanes−ethyl acetate) to give a mixture of diastereomeric hydroxy sulfides. Yield = 633 mg (1.69 mmol) = 77%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 6H), 0.97 (s, 9H), 1.25 (m, 2H), 1.80−2.00 (m, 3H), 3.83 (t, J = 6.5, 2H), 4.11 (m, 1H), 4.99 (m, 1H), 7.1−7.4 (m, 5H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.28 (2), 14.5, 15.1, 21.8 (2), 21.9 33.4, 47.0, 64.6, 65.1, 67.9, 75.2, 81.9, 87.3, 125.4, 126.6 (2), 127.1, 128.4, 135.9; MS m/z (M^+) calcd 374.1736, obsd 365.1633 (loss of H_2O). Anal. Calcd for $C_{21}H_{30}O_2SSi$: C, 67.33; H, 8.07. Found: C, 67.81; H, 7.95.

I.b. General Procedure Using Water/DMF (3:1 Mixture) as Solvent. A magnetically stirred solution of aldehyde (**3**) (2.2 mmol) in a solution of deionized water (16.5 mL) and DMF (5.5 mL) was treated with α-chloropropargyl phenyl sulfide (702 mg, 3.0 mmol) and indium powder (252 mg, 2.2 mmol). The solution was allowed to proceed at room temperature until no **3** was seen (TLC analysis).

(20) (a) Paquette, L. A.; Mitzel, T. M.; Isaac, M. B.; Crasto, C. F.; Schomer, W. M. *J. Org. Chem.* **1997**, *62*, 4293. (b) Sato, T.; Otera, J.; Nozaki, H. *J. Org. Chem.* **1990**, *55*, 6116. (c) Shimagaki, M.; Maeda, T.; Matsuzaki, Y.; Hori, I.; Nakata, T.; Oishi, T. *Tetrahedron Lett.* **1984**, *25*, 4775.

Dichloromethane was added, and stirring was maintained for 30 min. The layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with 1 N HCl until DMF was no longer present (generally about 3 × 20 mL washing). The organic layer was dried over $MgSO_4$ and evaporated to leave a dark yellow to brown oil. Purification was accomplished by flash chromatography or radial chromatography on silica gel (hexanes−ethyl acetate) to give a mixture of hydroxy sulfides[20] as a light yellow oil. No Cope product was witnessed under these conditions. The products were analyzed as shown in part I.a of the Experimental Section.

I.c. General Procedure Using DMF as Solvent. A magnetically stirred solution of aldehyde (**3**) (2.2 mmol) in DMF (22 mL) was treated with α-chloropropargyl phenyl sulfide (702 mg, 3.0 mmol) and indium powder (252 mg, 2.2 mmol). The solution was allowed to proceed at room temperature until no **3** was seen (TLC analysis). Dichloromethane (50 mL) and 1 N HCl (30 mL) were added, and stirring was maintained for 30 min. The layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with 1 N HCl until DMF was no longer present (generally about 3 × 20 mL washing). The organic layer was dried over $MgSO_4$ and evaporated to leave a brown oil. Separation of the 1,2-product and Cope product was not possible at this stage due to low yields. Ratios shown in Table 1 are based on a comparison of the NMR peaks in the regions shown below:



Mixture ratios, in general, between allene and alkyne products were determined by comparing the allene proton shift, which is approximately δ 6.0−6.5 ppm, and the terminal proton of the alkyne moiety, which occurs between δ 1.7−2.6 ppm depending on the nature of R.

II. Coupling Procedures for Propargyl Aldehyde (3) with Allyl Bromide. II.a. General Procedure Using Water as Solvent. A magnetically stirred solution of aldehyde (**3**) (2.2 mmol) in deionized water (22 mL) was treated with allyl bromide (357 mg, 3.0 mmol) and indium powder (252 mg, 2.2 mmol). The solution was allowed to proceed at room temperature until no **3** was seen (TLC analysis). Dichloromethane (30 mL) was added, and stirring was maintained for 30 min. The layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were dried over $MgSO_4$ and evaporated to leave a dark yellow to brown oil. Purification was accomplished by flash chromatography or radial chromatography on silica gel (hexanes−ethyl acetate) to give the alcohol as a light yellow oil. No Cope product was witnessed under aqueous conditions.

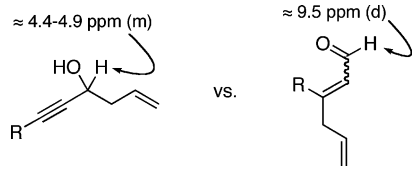
II.a.1. Use of 3-Trimethylsilypropynal (R = TMS) with Allyl Bromide.[21] Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (25:1 hexanes−ethyl acetate) to give the alcohol. Yield = 203 mg (1.21 mmol) = 55%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.17 (s, 9H), 2.48 (m, 2H), 4.42 (t, J = 6.4 Hz, 1H), 5.20 (m, 2H), 5.89 (m, 1H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.2 (3), 42.2, 62.2, 90.0, 106.1, 119.2, 133.0; MS m/z (M^+) calcd 168.0970, obsd 167.0913 (loss of H).

II.a.2. Use of Hept-2-ynal (R = *n*-Butyl) with Allyl Bromide.[22] Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (35:1 hexanes−ethyl acetate) to give the alcohol. Yield = 290 mg (1.91 mmol) = 87%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91−1.51 (m, 7H), 1.93 (t, J = 6.4 Hz, 2H), 2.28 (m, 2H), 4.45 (m, 1H), 5.12 (m, 2H), 5.75 (m, 1H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5, 16.4, 21.9, 32.0, 41.3, 65.8, 75.1, 79.6, 116.0, 136.9; MS m/z (M^+) calcd 152.1201, obsd 152.1201.

II.a.3. Use of 3-Phenylpropynal (R = Phenyl) with Allyl Bromide.[23] Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (35:1 hexanes−ethyl acetate) to give the alcohol. Yield = 340 mg (1.98 mmol) = 90%. Spectra were compared to that in ref 23.

II.a.4. Use of 6-(*tert*-Butyldimethylsiloxy)-2-hexynal (R = $(CH_2)_3$−OTBS) with Allyl Bromide.[22] Processing and analysis of this reaction proceeded as described in part I.a. Separation was accomplished using radial chromatography on silica gel (25:1 hexanes−ethyl acetate) to give the alcohol. Yield = 312 mg (1.17 mmol) = 53%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.25 (s, 6H), 0.97 (s, 9H), 1.31 (m, 2H), 2.00 (m, 2H), 2.31 (m, 2H), 3.80 (t, J = 6.6, 2H), 4.41 (m, 1H), 5.10 (m, 2H), 5.74 (m, 1H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.25 (2), 14.5, 15.1, 21.5 (3), 33.6, 41.3, 64.6, 67.3, 80.1, 92.4, 115.9, 136.9; MS m/z (M^+) calcd 268.1859, obsd 268.1832. Anal. Calcd for $C_{15}H_{28}O_2Si$: C, 67.11; H, 10.51. Found: C, 67.21; H, 10.51.

II.b. General Procedure Using DMF as Solvent. A magnetically stirred solution of aldehyde (**3**) (2.2 mmol) in DMF (22 mL) was treated with allyl bromide (357 mg, 3.0 mmol) and indium powder (252 mg, 2.2 mmol). The solution was allowed to proceed at room temperature until no **3** was seen (TLC analysis). Dichloromethane (50 mL) and 1 N HCl (30 mL) were added, and stirring was maintained for 30 min. The layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with 1 N HCl until DMF was no longer present (generally about 3 × 20 mL washing). The organic layer was dried over $MgSO_4$ and evaporated to leave a brown oil. Separation of the 1,2-product and the Cope product was not possible at this stage. Ratios shown in Table 2 are based on a comparison of the NMR peaks in the regions shown below:



II.c. General Procedure Using THF as Solvent. A magnetically stirred solution of aldehyde (**3**) (2.2 mmol) in THF (22 mL) was treated with allyl bromide (357 mg, 3.0 mmol) and indium powder (252 mg, 2.2 mmol). The solution was allowed to proceed at room temperature until no **3** was seen (TLC analysis). The stirring period for THF is generally 2−4 days in the absence of sonication. Dichloromethane (50 mL) and 1 N HCl (30 mL) were added, and stirring was maintained for 30 min. The layers were separated, and the aqueous phase was extracted with dichloromethane (2 × 10 mL). The combined organic layers were washed with 1 N HCl until THF was no longer present (generally 2 × 20 mL washing). The organic layer was dried over $MgSO_4$ and evaporated to leave a brown oil. Separation of the 1,2-product and the Cope product was

(21) For comparative NMR data: Burova, S. A.; McDonald, F. E. *J. Am. Chem. Soc.* **2004**, *124*, 8188.

(22) For comparative synthesis: Hartley, R. C.; Lamothe, S.; Chan, T. H. *Tetrahedron Lett.* **1993**, *34*, 1449.

(23) For spectral comparison: Mamane, V.; Gress, T.; Krause, H.; Furstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654.

not possible at this stage. Ratios shown in Table 2 are based on a comparison of the NMR peaks in the regions discussed in part II.b above.

III. Formation of Lactol (10) from Alcohol (3) Using KH (18-Crown-6). III.a. Formation of 6-(Hept-1-ynyl)-4-pentyl-5-vinyl-tetrahydro-2*H*-pyran-2-ol from Undec-1-ene-5-yn-4-ol (R = *n*-Pentyl). To a preweighed, flame dried, 250 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (720 mg, 18.0 mmol of KH). To this solid was added 50 mL of THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 20 mL solution of alcohol (762 mg, 4.59 mmol) and 18-crown-6 (1.192 g, 4.51 mmol) in THF were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction was quenched by dropwise addition of water (30 mL) over 30 min. The mixture was extracted with 2 × 25 mL of dichloromethane. The organic layers were combined and washed with 3 × 40 mL of 1 N HCl. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 25:1 hexanes−ethyl acetate as the eluent to give a mixture of two diastereomers as a light yellow oil.

There are two diastereomers present as seen by NMR. It is proposed that the alkyl groups are equatorial and the OH group is either equatorial or axial as shown below. No further spectral elucidation was conducted at this time. Yield = 617 mg (93% recovery, theoretical 100% recovery given fragmentation would be 664 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.9−1.00 (m, 6H), 1.2−1.50 (m, 15H), 1.7−1.75 (m, 1H), 2.20 (m, 2H), 2.46 (m, 2H), 4.40 (m, 1H), 4.78 (m, 0.4H), 5.03 (m, 0.6H), 5.20 (m, 2H), 5.80 (m, 1H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.9, 15.0, 19.7, 23.1 (2), 23.6, 29.5, 30.7, 31.5, 32.0, 32.5, 37.3, (41.3, 41.4), (66.5, 67.5), 77.7, 79.4, (90.4, 92.4), 118.0, 134.9; MS *m*/*z* (M^+) calcd 292.2402, obsd 274.2315 (loss of water). Anal. Calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 77.95; H, 11.09.

2-proposed diastereomers for the lactol (**10**)

III.b. Formation of 6-(Hex-1-ynyl)-4-butyl-5-vinyl-tetrahydro-2*H*-pyran-2-ol from Dec-1-ene-5-yn-4-ol (R = *n*-Butyl). To a preweighed, flame dried, 250 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL of THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (475 mg, 11.8 mmol of KH). To this solid was added 35 mL of THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 15 mL solution of alcohol (448 mg, 2.95 mmol) and 18-crown-6 (752 mg, 2.85 mmol) in THF were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction was quenched by dropwise addition of 20 mL of water over 30 min. The mixture was extracted with 2 × 20 mL of dichloromethane. The organic layers were combined and washed with 3 × 25 mL of 1 N HCl. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 25:1 hexanes−ethyl acetate as the eluent to give a mixture of two diastereomers as a light yellow oil. Yield = 342 mg (89% recovery, theoretical 100% recovery given fragmentation would be 385 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.9−1.10 (m, 6H), 1.2−1.50 (m, 11H), 1.7−1.75 (m, 1H), 2.22 (m, 2H), 2.47 (m, 2H), 4.45 (m, 1H), 4.82 (m, 0.4H), 5.10 (m, 0.6H), 5.21 (m, 2H), 5.80 (m, 1H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0 (2), 19.4, 23.0, 23.5, 23.6, 29.8, 30.5, 32.1, 32.3, (41.3, 41.4), (66.5, 67.6), 77.7, 79.3, (90.4, 92.5), 118.2, 135.0; MS *m*/*z* (M^+) calcd 264.2089, obsd 246.1873 (loss of water). Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.43; H, 10.75.

III.c. Formation of 4-Phenyl-6-(2-phenylethynyl)-5-vinyl-tetrahydro-2*H*-pyran-2-ol from 6-Phenyl-hex-1-ene-5-yn-4-ol (R = Phenyl). To a preweighed, flame dried, 100 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL of THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (313 mg, 7.83 mmol of KH). To this solid was added 30 mL of THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 10 mL solution of alcohol (334 mg, 1.94 mmol) and 18-crown-6 (525 mg, 1.99 mmol) in THF were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction was quenched by dropwise addition of 20 mL of water over 30 min. The mixture was extracted with 2 × 20 mL of dichloromethane. The organic layers were combined and washed with 3 × 25 mL of 1 N HCl. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 25:1 hexanes−ethyl acetate as the eluent to give a mixture of two diastereomers as a light yellow oil. Yield = 53 mg (18% recovery, theoretical 100% recovery given fragmentation would be 385 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60 (m, 1H), 2.71 (m, 3H), 4.69 (m, 1H), 4.91 (m, 0.4H), 5.15 (m, 0.6H), 5.20 (m, 2H), 5.95 (m, 1H), 7.2−7.6 (m, 10H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.1, 39.8, (41.2, 41.3), (66.9, 68.1), 78.4, 88.1, (91.0, 93.1), 118.9, 122.1, 123.6, 127.7, 128.3(2), 129.2, 129.4(2), 132.8(2), 134.4(2), 136.6; MS *m*/*z* (M^+) calcd 304.1463, obsd 286.1427 (loss of water). Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62. Found: C, 82.83; H, 6.58.

III.d. Formation of 6-Ethynyl-5-vinyl-tetrahydropyran-2-ol from 6-Trimethylsilyl-hexa-1-ene-5-yn-4-ol (R = TMS, in Starting Material Only, Cleaved during Reaction). To a preweighed, flame dried, 50 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL of THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (174 mg, 4.35 mmol of KH). To this solid was added 15 mL of THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 5 mL solution of alcohol (168 mg, 1.00 mmol) and 18-crown-6 (269 mg, 1.00 mmol) in THF were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction was quenched by dropwise addition of 15 mL of water over 30 min. The mixture was extracted with 2 × 15 mL of dichloromethane. The organic layers were combined and washed with 3 × 15 mL of 1 N HCl. It should be noted that the R_f of the product, as monitored by TLC, was reduced significantly during the workup phase, signifying removal of the TMS groups. We were unable to avoid cleavage of the TMS-group in our workup procedure using several methods. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 25:1 hexanes−ethyl acetate as the eluent to give a mixture of two diastereomers as a light yellow oil. Yield = 18

mg (25% recovery, theoretical 100% recovery given fragmentation would be 75 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (m, 2H), 2.46 (m, 2H), 2.58 (m, 2H), 4.45 (m, 1H), 4.85 (m, 0.3H), 5.11 (m, 0.7H), 5.25 (m, 2H), 5.90 (m, 1H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 38.1, (40.8, 40.9), (66.1, 67.2), 75.1, 83.1, (90.6, 92.9), 119.1, 134.2; MS *m*/*z* (M^+) calcd 152.0837, obsd 152.0833. Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 70.99; H, 8.01.

IV. Formation of Lactol (15) from Alcohol (13) Using KH (18-Crown-6). IV.a. Formation of 6-(Hex-1-ynyl)-4-butyl-5-(2-methylvinyl)-tetrahydro-2*H*-pyran-2-ol from 3-Methyl-dec-5-yne-1-ene-4-ol (R = *n*-Butyl). To a preweighed, flame dried, 200 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL of THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (695 mg, 17.3 mmol of KH). To this solid was added 50 mL of a 30% Et_2O solution in THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 20 mL solution (30% Et_2O in THF) of alcohol (762 mg, 4.59 mmol) and 18-crown-6 (1.192 g, 4.51 mmol) were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction mixture was quenched by dropwise addition of 30 mL of water over 30 min. The mixture was extracted with 2 × 25 mL of dichloromethane. The organic layers were combined and washed with 3 × 40 mL of 1 N HCl. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 30:1 hexanes−ethyl acetate as the eluent to give a mixture of two diastereomers as a light yellow oil. Yield = 57 mg (9.5% recovery, theoretical 100% recovery given fragmentation would be 598 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90−1.00 (m, 6H), 1.20−1.50 (m, 11H), 1.71−1.79 (m, 4H), 2.11 (m, 2H), 2.43 (m, 2H), 4.45 (m, 1H), 4.87 (M, 04.H), 5.10 (m, 0.6H), 5.55−5.70 (m, 2H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6 (2), 17.5, 19.1, 22.4, 22.9, 23.1, 30.5 (2), 31.0, 37.2, (40.9, 41.2), (65.9, 66.2), 76.9, 77.4, (90.4, 92.1), 124.2, 133.7; MS *m*/*z* (M^+) calcd 278.2246, obsd 260.2142 (loss of water). Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.73; H, 10.81.

IV.b. Formation of 4-Phenyl-6-(2-phenylethynyl)-5-(2-methylvinyl)-tetrahydro-2*H*-pyran-2-ol from 3-Methyl-6-phenyl-hex-5-yne-1-ene-4-ol (R = Phenyl). To a preweighed, flame dried, 100 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL of THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (270 mg, 6.75 mmol of KH). To this solid was added 30 mL of a 30% Et_2O solution in THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 10 mL (30% Et_2O solution in THF) solution of alcohol (314 mg, 1.69 mmol) and 18-crown-6 (449 g, 1.70 mmol) were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction was quenched by dropwise addition of 15 mL of water over 30 min. The mixture was extracted with 2 × 15 mL of dichloromethane. The organic layers were combined and washed with 3 × 20 mL of 1 N HCl. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 20:1 hexanes−ethyl acetate as the eluent to give a mixture of two diastereomers as a light yellow oil. Yield = 24 mg (8.8% recovery, theoretical 100% recovery given fragmentation would be 270 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.65 (m, 1H), 1.74 (m, 3H), 2.70−2.75 (m, 3H), 4.68 (m, 1H), 4.95 (m, 0.4H), 5.16 (m, 0.6H), 5.50−5.80 (m, 2H), 7.2−7.6 (m, 10H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0, 28.0, 37.5, (40.9, 41.5), (66.2, 67.4), 78.3, 88.1, (90.9, 93.1), 122.6, 124.2, 125.8, 128.1, 128.3 (2), 128.5 (2), 128.6, 128.9, 132.1, 132.2, 133.1, 138.4; MS *m*/*z* (M^+) calcd 318.1620, obsd 300.1514 (loss of water). Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.99; H, 6.96. Found: C, 83.20; H, 6.89.

V. Formation of Lactol (16) from Alcohol (14) Using KH (18-Crown-6). V.a. Formation of 6-(Hex-1-ynyl)-4-butyl-5-methyl-5-vinyl-tetrahydro-2*H*-pyran-2-ol from Undec-6-yne-2-ene −5-ol (R = *n*-Butyl). To a preweighed, flame dried, 200 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL of THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (765 mg, 19.1 mmol of KH). To this solid was added 50 mL of a 30% Et_2O solution in THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 20 mL solution (30% Et_2O in THF) of alcohol (790 mg, 4.78 mmol) and 18-crown-6 (1.261 g, 4.78 mmol) were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction was quenched by dropwise addition of 30 mL of water over 30 min. The mixture was extracted with 2 × 25 mL of dichloromethane. The organic layers were combined and washed with 3 × 40 mL of 1 N HCl. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 30:1 hexanes−ethyl acetate as the eluent to give a light yellow oil. More than one diastereomer was present by NMR, but they were not separated at this stage. Yield = 296 mg (45% recovery, theoretical 100% recovery given fragmentation would be 657 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90−1.10 (m, 6H), 1.15−1.50 (m, 14H), 2.08 (m, 2H), 2.38 (m, 2H), 4.39 (m, 1H), 4.95 (m, 0.5H), 5.10 (m, 0.5H), 5.25−5.60 (m, 2H), 5.85−5.95 (m, 1H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.1, (15.1, 15.3), 19.1, 21.6, 22.7, 25.6, 30.4, 31.3 (2), 39.5, (40.2, 40.4), (66.2, 67.5), 75.8, 77.2, (91.2, 93.7), 116.2, 137.8; MS *m*/*z* (M^+) calcd 278.2246, obsd 278.2149. Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 78.01; H, 10.74.

V.b. Formation of 4-Phenyl-6-(2-phenylethynyl)-5-methyl-5-vinyl-tetrahydro-2*H*-pyran-2-ol from 7-Phenyl-hept-6-yne-2-ene-5-ol (R = Phenyl). To a preweighed, flame dried, 200 mL, three-necked flask equipped with a magnetic stir bar was added a KH−mineral oil mixture. The mixture was washed with 3 × 5 mL of THF to remove the mineral oil. The flask was placed under high vacuum (0.002 mmHg) to remove solvent traces leaving KH as a gray solid, which was then weighed (630 mg, 15.75 mmol of KH). To this solid was added 50 mL of a 30% Et_2O solution in THF, and the resulting mixture was cooled to −78 °C under an argon atmosphere. A 20 mL solution (30% Et_2O in THF) of alcohol (732 mg, 3.94 mmol) and 18-crown-6 (1.040 g, 3.95 mmol) were added to the KH mixture with stirring over a 5−10 min period. The resulting solution was allowed to warm to −40 °C over a period of 1.5 h, then allowed to warm to 0 °C over an additional 1 h. The reaction was quenched by dropwise addition of 30 mL of water over 30 min. The mixture was extracted with 2 × 25 mL of dichloromethane. The organic layers were combined and washed with 3 × 40 mL of 1 N HCl. The organic layers were dried over $MgSO_4$, and the solvent was removed in vacuo to give the crude product as a brown oil. The crude product was purified by radial chromatography on silica gel using 30:1 hexanes−ethyl acetate as the eluent to give a light yellow oil. More than one diastereomer was present by NMR, but they were not separated at this stage. Yield = 94 mg (15% recovery, theoretical 100% recovery given fragmentation would be 626 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (s, 1.5H), 1.07 (s, 1.5H), 2.70−2.75 (m, 3H), 4.58 (m, 1H), 4.91 (m, 0.5H), 5.18 (m, 0.5H), 5.21 (m, 2H), 5.93 (m, 1H), 7.20−

7.61 (m ,10H), the OH proton was not detected; ^{13}C NMR (75 MHz, $CDCl_3$) δ (15.3, 15.5), 34.0, 39.5, (40.2, 40.7), (65.9, 67.1), 77.9, 88.2, (89.9, 90.6), 115.3, 122.1, 125.7, 126.8 (2), 128.4 (2), 128.7, 128.8, 128.9, 130.2 (2), 137.5, 141.0; MS *m*/*z* (M^+) calcd 318.1620, obsd 318.1620. Anal. Calcd for $C_{22}H_{22}O_2$: C, 82.99; H, 6.96. Found: C, 82.78; H, 7.05.

VI. Formation of Formate Ester (17) from Aldehyde (3) in *N*-Methylformamide. VI.a. Formation of Undec-5-yn-1-ene-4-ol, Formate Ester from Octynal. To a 100 mL round-bottomed flask was added 55 mL of NMF along with octynal (622 mg, 5.02 mmol), allyl bromide (912 mg, 7.54 mmol), and indium powder (634 mg, 5.52 mmol). The flask was capped with a rubber stopper, and the mixture was sonicated for 72 h, at which time TLC revealed the reaction was no longer progressing. Sonication was stopped, and 60 mL of dichlormethane was added to the product mixture with stirring for 30 min. Water (40 mL) was added with stirring for 10 min, and the layers separated. A 1 N HCl solution (25 mL) was added to the organic layer with stirring for 10 min at which time the layers were separated. The organic layer was washed with 2 × 20 mL of a 1 N HCl solution. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo to give a yellow liquid. Purification was performed using radial chromatography (silica gel, 25:1 hexanes−ethyl acetate) to give the formate ester as a light yellow oil. Yield = 613 mg (3.16 mmol) = 63%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.83 (t, J = 7.3 Hz, 3H), 1.27 (m, 4H), 1.44 (m, 2H), 2.14 (m, 2H), 2.47 (m, 2H), 5.11 (m, 2H), 5.44 (t, J = 5.9 Hz, 1H), 5.76 (m, 1H), 8.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0, 19.6, 23.2, 29.1, 32.0, 40.5, 64.6, 77.5, 88.6, 119.6, 133.2, 161.0; MS *m*/*z* (M^+) calcd 194.1307, obsd 194.1315. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.83; H, 8.99.

VI.b. Formation of 6-Phenyl-hex-5-yn-1-en-4-ol, Formate Ester from 3-Phenylpropynal. To a 100 mL round-bottomed flask was added 55 mL of NMF along with 3-phenylpropynal (585 mg, 4.50 mmol), allyl bromide (810 mg, 6.75 mmol), and indium powder (574 mg, 5.00 mmol). The flask was capped with a rubber stopper, and the mixture was sonicated for 72 h, at which time TLC revealed the reaction was no longer progressing. Sonication was stopped, and 50 mL of dichlormethane was added to the product mixture with stirring for 30 min. Water (35 mL) was added with stirring for 10 min, and the layers separated. A 1 N HCl solution (20 mL) was added to the organic layer with stirring for 10 min at which time the layers were separated. The organic layer was washed with 2 × 20 mL of 1 N HCl solution. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo to give a yellow liquid. Purification was performed using radial chromatography (silica gel, 30:1 hexanes−ethyl acetate) to give the formate ester as a light yellow oil. Yield = 540 mg (2.70 mmol) = 60%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (m, 2H), 5.14 (m, 2H), 5.51 (t, J = 5.7 Hz, 1H), 5.92 (m, 1H), 7.2−7.4 (m, 5H), 8.06 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.5, 65.1, 77.3, 90.5, 118.3, 122.7, 128.1, 128.3, 128.4, 131.0, 132.3, 135.6, 161.3; MS *m*/*z* (M^+) calcd 200.0837, obsd 200.0824. Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 78.21; H, 6.15.

VI.c. Formation of 6-Trimethylsilyl-hex-yn-4-1-en-4-ol, Formate Ester from 3-Trimethylsilylpropynal. To a 50 mL round-bottomed flask was added 30 mL of NMF along with 3-trimethylsilylpropynal (324 mg, 2.57 mmol), allyl bromide (462 mg, 3.85 mmol), and indium powder (324 mg, 2.82 mmol). The flask was capped with a rubber stopper, and the mixture was sonicated for 84 h at which time TLC revealed the reaction was no longer progressing. Sonication was stopped, and 30 mL of dichlormethane was added to the product mixture with stirring for 30 min. Water (15 mL) was added with stirring for 10 min, and the layers separated. A 1 N HCl solution (10 mL) was added to the organic layer with stirring for 10 min at which time the layers were separated. The organic layer was washed with 2 × 10 mL of 1 N HCl solution. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo to give a yellow liquid. The crude product was purified using radial chromatography (silica gel, 20:1 hexanes−ethyl acetate) to give the formate ester as a light yellow oil. Yield = 317 mg (1.62 mmol) = 63%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.17 (s, 9H), 2.48 (m, 2H), 5.20 (m, 2H), 5.48 (t, J = 6.3 Hz, 1H), 5.87 (m, 1H), 8.07 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.2(3), 41.7, 62.6, 89.3, 106.1, 119.2, 133.8, 160.9; MS *m*/*z* (M^+) calcd 196.0920, obsd 196.0913. Anal. Calcd for $C_{10}H_{16}O_2$: C, 61.18; H, 8.21. Found: C, 60.99; H, 8.15. It should be noted that there was approximately 15% of the formate formed in which the TMS group had been removed. This isomer was noted via NMR and MS of the crude material but was not isolated further.

VI.d. Formation of Dec-5-yn-1-ene-4-ol, Formate Ester from Heptynal. To a 100 mL round-bottomed flask was added 60 mL of NMF along with octynal (605 mg, 5.50 mmol), allyl bromide (990 mg, 8.25 mmol), and indium powder (694 mg, 6.05 mmol). The flask was capped with a rubber stopper, and the mixture was sonicated for 72 h at which time TLC revealed the reaction was no longer progressing. Sonication was stopped, and 60 mL of dichlormethane was added to the product mixture with stirring for 30 min. Water (40 mL) was added with stirring for 10 min, and the layers separated. A 1 N HCl solution (25 mL) was added to the organic layer with stirring for 10 min at which time the layers were separated. The organic layer was washed with 2 × 20 mL of 1 N HCl solution. The organic layer was dried over $MgSO_4$, and the solvent was removed in vacuo to give a yellow liquid. Purification was performed using radial chromatography (silica gel, 25:1 hexanes−ethyl acetate) to give the formate ester as a light yellow oil. Yield = 642 mg (3.57 mmol) = 65%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, J = 7.4 Hz, 3H), 1.31 (m, 2H), 1.47 (m, 2H), 2.17 (m, 2H), 2.44 (m, 2H), 5.15 (m, 2H), 5.47 (t, J = 6.1 Hz, 1H), 5.80 (m, 1H), 8.02 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2, 19.4, 23.5, 32.1, 40.4, 65.2, 77.5, 88.3, 119.4, 133.4, 161.7; MS *m*/*z* (M^+) calcd 180.1150, obsd 180.1161. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.47; H, 8.96.

VII. Formation of Cope Product (9) from Alcohol (3). VII.a. Formation of 3-Pentyl-hexa-2,5-dienal from 2-Octynal. To a 25 mL round-bottomed flask was added a solution of 5.5 mL of NMF and 5.5 mL of DMSO. To this solution was added 2-octynal (124 mg, 1 mmol), allyl bromide (180 mg, 1.5 mmol), indium powder (126 mg, 1.1 mmol), and $InCl_3$ (219 mg, 1.0 mmol). The mixture was sonicated for 84 h at which time TLC showed no further changes in the product mixture. At this stage, sonication was stopped, and dichloromethane (40 mL) was added with stirring for 30 min. To the resulting mixture was added 25 mL of 1 N HCl with stirring for 30 min. The layers were separated, and the organic layer was washed with 3 × 15 mL of 1 N HCl, then dried over $MgSO_4$. Purification was performed using radial chromatography (silica gel, 25:1 hexanes−ethyl acetate) to give the aldehyde as a mixture of diastereomers. Yield = 58 mg (0.35 mmol) = 35%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (m, 3H), 1.28 (m, 6H), 1.90 (m, 2H), 2.57 (m, 2H), 5.15 (m, 2H), 5.72 (m, 1H), 5.82 (m, 1H), 9.51 (d, J = 7.7 Hz, 0.5H), 9.54 (d, J = 7.7 Hz, 0.5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0, 22.5, 24.7, 31.7, 32.1, 40.4, 115.1, 126.1, 134.9, 163.3, (193.1, 193.2); MS *m*/*z* (M^+) calcd 166.1358, obsd 166.1339. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 78.91; H, 10.33.

VII.b. Formation of 3-Butyl-hexa-2,5-dienal from 2-Heptynal. Processing and analysis of this reaction proceeded as described in part VI.a. Purification was accomplished using radial chromatography on silica gel (25:1 hexanes−ethyl acetate) to give the aldehyde as a mixture of diastereomers. Yield = 51 mg (0.34 mmol) = 34%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (m, 3H), 1.41 (m, 4H), 1.91 (m, 2H), 2.57 (m, 2H), 5.17 (M, 2H), 5.69 (m, 1H), 5.85 (m, 1H), 9.51 (d, J = 7.7 Hz, 0.5 H), 9.53 (d, J = 7.7 Hz, 0.5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.8, 22.7, 31.2, 31.9, 40.6,

115.9, 125.3, 134.8, 161.1, (191.0, 191.3); MS *m*/*z* (M^+) calcd 152.1201, obsd 152.1239. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.50; H, 10.27. Bp = 85−87 °C at 12 Torr.[24]

VII.c. Formation of 3-Phenyl-hexa-2,5-dienal from 3-Phenyl-propynal. Processing and analysis of this reaction proceeded as described in part VI.a. Purification was accomplished using radial chromatography on silica gel (30:1 hexanes−ethyl acetate) to give the aldehyde as a mixture of diastereomers. Yield = 46 mg (0.27 mmol) = 27%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.63 (m, 2H), 5.15 (m, 2H), 5.85 (m, 1H), 5.90 (m, 0.5H), 6.30 (m, 0.5H), 7.19 (m, 3H), 7.35 (m, 2H), 9.63 (d, J = 7.6 Hz, 0.5H), 9.68 (d, J = 7.7 Hz, 0.5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.9, 115.1, 123.0, 126.3-(2), 127.3, 128.1, 128.4, 134.7, 135.1, (159.6, 159.8), (190.0, 190.2); MS *m*/*z* (M^+) calcd 172.0888, obsd 171.9998. Anal. Calcd for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 84.01; H, 6.85.

(24) Ullrich, F. W.; Rotscheidt, K.; Breitmaier, E. *Chem. Ber*. **1986**, *119*, 1737.

(25) For comparitive syntheses: (a) Mandai, T.; Arase, H.; Otera, J.; Kawada, M. *Tetrahedron Lett.* **1985**, *26*, 2677. (b) Otera, J.; Mandai, T.; Shiba, M.; Saito, T.; Shimohata, K.; Takemori, K.; Kawasaki, Y. *Organometallics* **1983**, *2*, 332.

VII.d. Formation of 3-Trimethylsilyl-hexa-2,5-dienal from 3-Trimethylsilyl-propynal. Processing and analysis of this reaction proceeded as described in part VI.a. Purification was accomplished using radial chromatography on silica gel (50:1 hexanes−ethyl acetate) to give the aldehyde as a mixture of diastereomers. Yield = 49 mg (0.29 mmol) = 29%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.17 (s, 9H), 2.60 (m, 2H), 5.21 (m, 2H), 5.85 (m, 1H), 6.27 (m, 0.7H), 6.58 (m, 0.3H), 9.64 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (0.1, 0.3)[3], (35.3, 37.1), 115.0, 133.6, 140.1, (160.1, 160.2), (192.9, 193.1); MS *m*/*z* (M^+) calcd 168.0970, obsd 168.0968. Anal. Calcd for $C_{19}H_{16}OSi$: C, 64.23; H, 9.58. Found: C, 64.51; H, 9.69.[25]

Acknowledgment. Financial support received from the National Science Foundation-REU granting program, Pfizer Undergraduate Research Award Grant, the Howard Hughes Medical Association, and the Trinity College Internal Grant Foundation is greatly acknowledged.

JO070020K