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Olefination of α,α′-Divinyl Ketones through Catalytic Meyer−Schuster Rearrangement

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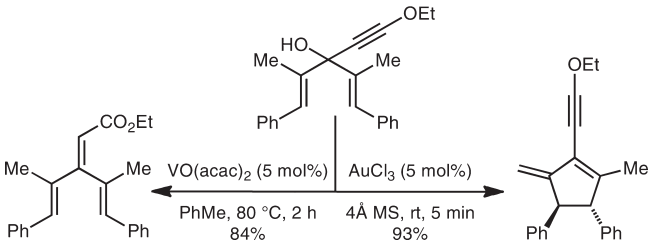

The direct olefination of 1,4-dien-3-ones remains a synthetic challenge. A two-step protocol, employing acetylide addition followed by catalytic Meyer−Schuster rearrangement has been developed for the olefination of 1,4-pentadien-3-ones to afford [3]dendralenes. Many of the traditional methods for the Meyer−Schuster rearrangement of alkynyl carbinols are not suitable with these highly unsaturated substrates because of their acid sensitivity. Unexpected reactivity during attempted rearrangement, including Nazarov-type electrocyclizations, is presented, along with conditions to promote the Meyer−Schuster rearrangement of ethoxyacetylene adducts using catalytic $VO(acac)_2$.

Introduction

Recently, there has been a resurgence in interest in the Meyer−Schuster rearrangement,[1] a process in which propargyl alcohols are converted into α,β-unsaturated carbonyl compounds through a formal 1,3-oxygen transposition.[2] Increased focus on this venerable reaction may be attributed to its potential use as part of a two-step olefination process through combination with a prior alkynyl anion addition to an aldehyde or ketone acceptor. An important feature of this transformation is its applicability to hindered ketones that are unreactive under traditional olefination conditions. Moreover, the atom-economy of the overall process is attractive.

Our interest in the reaction arose from efforts to develop a "vinylogous Nazarov reaction" (Scheme 1).[3] One of the early challenges encountered in this study centered around formation of the requisite cross-conjugated trienes ([3]dendralenes) **1**.[4] The most direct method would appear to be a Wittig or Horner−Wadsworth−Emmons-type olefination of the cross-conjugated dienones **4** used in the traditional Nazarov electrocyclization. However, a combination of steric hindrance and electronic deactivation precludes use of such a direct olefination process.

[3]Dendralenes and their higher order counterparts can be prepared through dibromoolefination/cross-coupling protocols using various aldehydes.[4e−g] Unfortunately, in our hands, this approach suffered poor yields and limited substrate scope in generating the carbonyl-substituted [3]dendralenes we

(1) (a) Lopez, S. S.; Engel, D. A.; Dudley, G. B. *Synlett* **2007**, 949–953. (b) Marion, N.; Carlqvist, P.; Gealageas, R.; de Frémont, P.; Maseras, F.; Nolan, S. P. *Chem.—Eur. J.* **2007**, *13*, 6437–6451. (c) Lee, S. I.; Baek, J. Y.; Sim, S. H.; Chung, Y. K. *Synthesis* **2007**, 2107–2114. (d) Engel, D. A.; Lopez, S. S.; Dudley, G. B. *Tetrahedron* **2008**, *64*, 6988–6996. (e) Trost, B. M.; Livingston, R. C. *J. Am. Chem. Soc.* **2008**, *130*, 11970–11978. (f) Engel, D. A.; Dudley, G. B. *Org. Biomol. Chem.* **2009**, *7*, 4149–4158. (g) Cadierno, V.; Frandos, J.; Gimeno, J. *Tetrahedron Lett.* **2009**, *50*, 4773–4776.

(2) (a) Meyer, K. H.; Schuster, K. *Chem. Ber.* **1922**, *55*, 819–823. (b) Vartanyan, S. A.; Babanyan, S. O. *Russ. Chem. Rev.* **1967**, *36*, 670–686. (c) Swaminat, S.; Narayana, K. V. *Chem. Rev.* **1971**, *71*, 429–438. (d) Cadierno, V.; Crochet, P.; Garcia-Garrido, S. E.; Gimeno, J. *Dalton Trans.* **2010**, *39*, 4015–4031.

(3) Rieder, C. J.; Winberg, K. J.; West, F. G. *J. Am. Chem. Soc.* **2009**, *131*, 7504–7505.

(4) Reviews on [3]dendralenes: (a) Hopf, H. *Angew. Chem., Int. Ed.* **1984**, *23*, 947–960. (b) Gholami, M.; Tykwinski, R. R. *Chem. Rev.* **2006**, *106*, 4997–5027. For recent synthetic approaches, see: (c) Fielder, S.; Rowan, D. D.; Sherburn, M. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 4331–433. (d) Chin, C. S.; Lee, H.; Park, H.; Kim, M. *Organometallics* **2002**, *21*, 3889–3896. (e) Park, S.; Lee, D. *Synthesis* **2007**, 2313–2316. (f) Bradford, T. A.; Payne, A. D.; Willis, A. C.; Paddon-Row, M. N.; Sherburn, M. S. *Org. Lett.* **2007**, *9*, 4861–4864. (g) Miller, N. A.; Willis, A. C.; Paddon-Row, M. N.; Sherburn, M. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 937–940.

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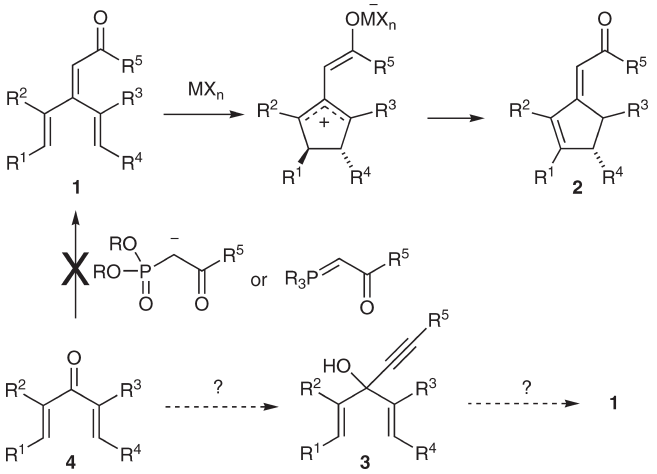
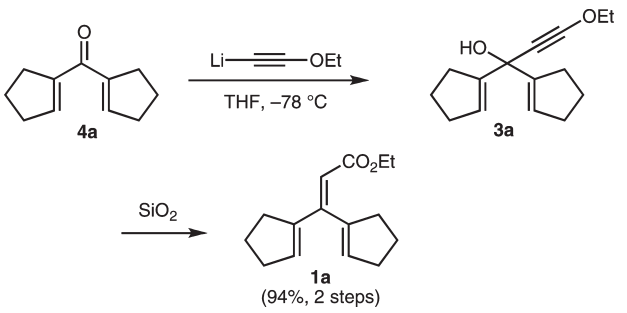
SCHEME 1. Vinylogous Nazarov Reaction



SCHEME 2. Acetylide Addition and Silica-Mediated Cyclization



sought. A variety of other multistep sequences and rearrangements were also attempted to generate the cross-conjugated trienes we desired but were met with minimal success. During these investigations, we became aware of a report of olefinations through a two-step sequence employing acetylide additions to hindered ketones followed by their subsequent Meyer–Schuster rearrangement under gold(III) catalysis.[5] Of particular interest was an example employing verbenone, a hindered, unsaturated ketone. This suggested an alternative approach to the desired dendralenes from dienones **4** via this two-step sequence. Here we describe the results of this study, including an efficient olefination strategy to afford sensitive [3]dendralenes substituted with ester groups on the central alkene and a variety of unexpected premature cyclization processes encountered during attempted Meyer–Schuster rearrangement of the initial alkyne adducts. To the best of our knowledge, these are the first successful examples making use of α,α′-divinyl propargylic alcohols in the Meyer–Schuster rearrangement.[6]

Results and Discussion

Prior to the present work, we had observed very few successful examples of 1,2-addition of organometallic reagents to 1,4-pentadien-3-ones, mainly involving allylmagnesium halides.[7] Success in these cases was attributed to prior complexation of Mg^{2+} to the carbonyl oxygen and addition with allylic inversion through a six-centered transition state. However, lithium acetylides were expected to be highly effective nucleophiles[7b] to afford the corresponding propargyl bis(allylic) alcohols. Facile addition by acetylides would result from the minimal steric demand of these cyclindrically symmetric anions.

In the event, initial efforts focused on the highly reactive lithium salt of ethoxyacetylene and dicyclopentenyl ketone **4a** (Scheme 2). Acetylide addition proceeded without incident to furnish propargyl alcohol **3a** in high yield. However, to our surprise, during attempted purification on silica gel, **3a** underwent Meyer–Schuster rearrangement to trienoate **1a** in excellent yield, presumably via catalysis by the mildly acidic silica. In fact, pretreatment of this sorbent with Et_3N cosolvent effectively inhibited the rearrangement. Unfortunately, this convenient transformation did not prove to be general, with most other adducts **3** found to be unreactive during chromatography or extended stirring over silica gel.

Given the lack of generality for the silica-mediated rearrangement, we turned our attention to other methods to effect Meyer–Schuster rearrangement of dienone–acetylide adducts. Propargyl alcohol **3b**, obtained in near-quantitative yield from dibenzylidene-3-pentanone **4b** and ethoxyacetylene, was inert to silica gel and was chosen as a model substrate to optimize the Meyer–Schuster rearrangement. Our initial focus was on the use of gold(III) chloride in light of the promising results in Dudley's early report (Table 1, entries 1–3). Indeed, treatment of **3b** under gold(III) catalysis gave the desired trienoate; however, the reaction was capricious and frequently furnished significant quantities of cycloisomerized byproducts such as **2b** or **5b**.

As a result of the high degree of variability of reactivity observed with gold(III) chloride, other promoters were examined to effect the Meyer–Schuster rearrangement. Aqueous HCl (entry 4) and other π-acids,[8] such as gold(I), silver, and platinum salts (entries 5–7), were explored and met with minimal success. Gallium(III) chloride and hexachloroplatinic acid, due to their extreme hygroscopicity, gave rise to significant quantities of hydration product **8b** (entries 8 and 9). While the use of $TiCl_4$ as an acid promoter in the Meyer–Schuster rearrangement worked exceptionally well in select cases (Scheme 3), the results did not generalize to all substrates. With **3b**, $TiCl_4$ not only provided the requisite triene but also effected vinylogous Nazarov ring closure to give **2b** (entry 10). Metal oxides gave variable yields of the desired trienoate **1b** (entries 12–14), with the greatest reproducibly obtained using the cost-effective $VO(acac)_2$.

Exposure of **3b** to $AuCl_3$ at elevated temperature immediately gave rise to significant amounts of **5b**. Prolonged exposure led to the formation of **6b** at the expense of **5b**. This appears to likely be the result of simple acid-mediated isomerization[9] to the more thermodynamically stable endocyclic olefin. Finally, treatment of **3b** with TsOH (entry 11) gave

(5) Engel, D. A.; Dudley, G. B. *Org. Lett.* **2006**, *8*, 4027–4029.

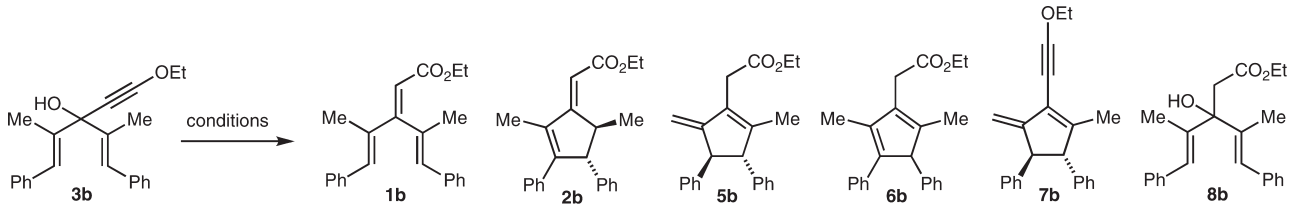
(6) Some previous attempted Meyer–Schuster reactions employing α-vinyl propargylic alcohols were not successful, possibly due to the accessibility of other competing acid-mediated processes: Yoshimatsu, M.; Naito, M.; Kawahigashi, M.; Shimizu, H.; Kataoka, T. *J. Org. Chem.* **1995**, *60*, 4798–4802.

(7) (a) Bender, J. A.; Winberg, K. J.; West, F. G. Unpublished results. (b) Magnesium acetylides were also examined and found to give mixtures of 1,2- and 1,4-addition products.

(8) (a) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410–3449. (b) Lee, S. I.; Chatani, N. *Chem. Commun* **2008**, 371–384. (c) Yamamoto, Y.; Gridnev, I. D.; Patil, N. T.; Jin, T. *Chem. Commun* **2009**, 5075–5087.

(9) For evidence of $AuCl_3$ acting as an H^+ source, see: Wabnitz, T. B.; Yu, J.-Q.; Spencer, J. B. *Chem.—Eur. J.* **2004**, *10*, 484–493.

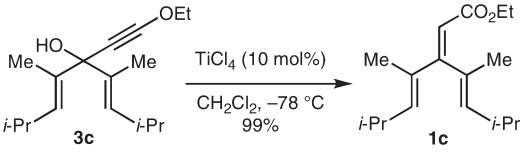
TABLE 1. Catalyst Screening



						% yield[a]					
entry	catalyst	loading (mol %)	solvent	*T* (°C)	time (h)	**1b**	**2b**	**5b**	**6b**	**7b**	**8b**
1	$AuCl_3$/EtOH	5/1000	CH_2Cl_2	rt	2 min	*10*		*90*			
2	$AuCl_3$	2	THF	50	2 min			63			
3	$AuCl_3$	2	THF	rt	16				62		
4	1 M HCl	1000	CH_2Cl_2	rt	48	*10*	*20*		*70*		
5	$AuClPPh_3$	5	THF	rt	24[b]	*70*		*20*	*10*		
6	$AuClPPh_3/AgSbF_6$	5/5	THF	rt	2 min	*9*	*8*	*33*	*50*		
7	$PtCl_4$	5	THF	rt	2			60			
8	10% H_2PtCl_6	40	THF	rt	2	30					42
9	$GaCl_3$	100	THF	rt	2	28					46
10	$TiCl_4$	10	CH_2Cl_2	−78	3	36	42				
11	TsOH	5	PhMe	rt	2					62	
12	$TiO(acac)_2$	5	PhMe	80	2	18					5
13	$VO(Oi\text{-}Pr)_3$	5	PhMe	80	2	56					
14	$VO(acac)_2$	5	PhMe	80	2	84					

[a]Yields for entries 1−4 are based on ratios measured in crude NMR spectra of the product mixtures. Yields for entries 5−14 are for isolated products after chromatographic purification. [b]Reaction proceeded to only 20% conversion, even after 24 h.

SCHEME 3. $TiCl_4$-Catalyzed Meyer−Schuster Reaction

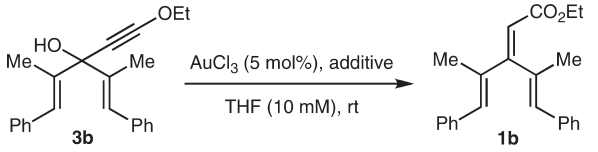


alkynylcyclopentene **7b**, formally the result of sequential dehydration/Nazarov cyclization. This result is particularly interesting, as it indicates that electrocyclization can proceed faster than Meyer−Schuster rearrangement under dehydrative conditions and suggests a possible mechanistic scheme to explain the formation of various cyclized byproduct (vide infra).

The effect of various additives on the gold-catalyzed process was evaluated (Table 2). Addition of electron-rich carbonyl compounds or silver salts was of little benefit, giving complex mixtures of products. On the other hand, exogenous water was found to enhance the rate of conversion to enoate. This observation is in accord with Dudley's proposed mechanism,[1d] in which added alcohol was found to be beneficial by means of apparent formation an intermediate ketene acetal. Oddly, the use of EtOH as a cosolvent in CH_2Cl_2 gave predominately **6b**. The reason for the discrepancy in the effect of ethanol and water additives remains obscure.

In contrast to the results of added water, inclusion of molecular sieves resulted in none of the desired trienoate **1b**, instead providing cyclized alkyne **7b** in high yield. Notably, exposure of **7b** to the normal reaction conditions resulted in hydration of the alkyne and alkene isomerization to yield **6b** as the only isolable product. This outcome implicates **7b** as a possible intermediate in the undesired pathway to **2b**, **5b**, and **6b**. If the premature cyclization products result from dehydration of **3b**, then acid scavengers would be expected to suppress this pathway. Indeed, the addition of Hünig's base or 2,6-lutidine quelled the byproduct formation, but at the cost of significantly increased reaction times.

TABLE 2. Additive Effects in $AuCl_3$-Catalyzed Reactions

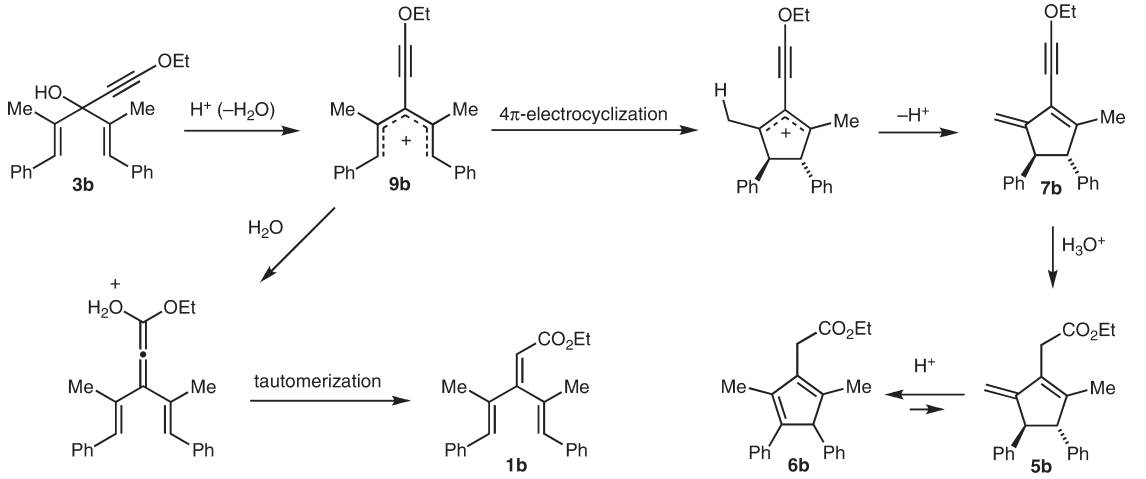


additive	loading	time	% yield[a]
None		2 min to 2 h	variable
$AgBF_4$	15 mol %	30 min	intractable
$AgSbF_6$	10 mol %	30 min	intractable
EtOAc	10 equiv	30 min	intractable
cyclohexanone	10 equiv	30 min	intractable
EtOH	10 equiv	30 min	1: 9[b]
H_2O	1 equiv	5 min	70
i-Pr_2NEt	10 mol %	24 h	53
2,6-lutidine	10 mol %	24 h	51
4 Å MS		5 min	93[c]

[a]Isolated yield after purification. [b]Ratio refers to **1b**:**6b** measured via integration of the ^1H NMR spectrum of the crude reaction mixture. Nearly identical results were obtained with CH_2Cl_2 as the solvent. [c]Refers to the isolated yield of **7b**.

Given the results above, we propose a dehydrative mechanism for the formation of cycloisomerized byproduct (Scheme 4). Protonation of the teriary alcohol of **3b** and subsequent loss of water would afford the corresponding pentadienyl cation **9b**. Conrotatory ring closure and elimination would furnish **7b**.[10] Hydration of the resulting alkyne would provide **5b**, which could then isomerize to **6b**. The formation of varying amounts of the trienoate under these

SCHEME 4. Proposed Dehydrative Mechanism



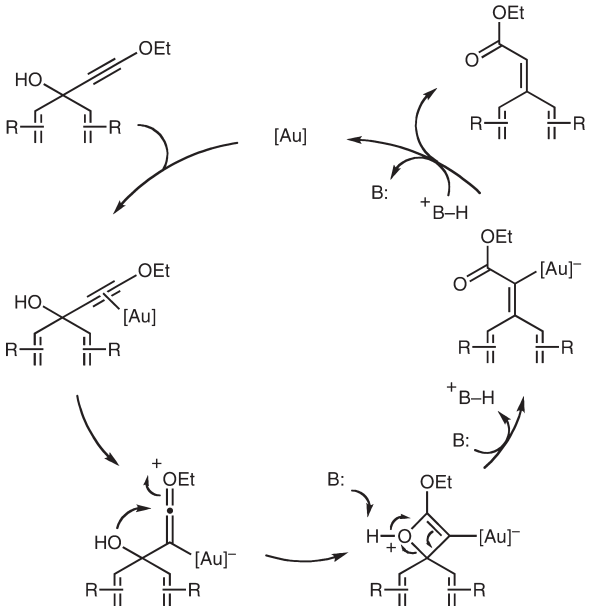
conditions is presumed to result from hydration of the initially formed the cation **9b** at the oxygenated terminus and subsequent tautomerization to **1b**.

Suppression of cycloisomerization upon the addition of base suggests that successful gold-mediated Meyer−Schuster rearrangement would avoid dehydration as the initial step, thereby avoiding the reactive pentadienyl cation **9b**. Activation of the alkyne by gold(III) could allow for intramolecular nucleophilic attack by the free alcohol to afford a gold-substituted oxetene intermediate (Scheme 5) or attack by water in those cases employing added water.[11] Opening of the oxetene would yield a gold trienoate which, following protonolysis, would afford the observed trienoate.

Despite the observation of occasional higher yields with gold(III) catalysis, the capricious nature of those reactions with these highly conjugated substrates compelled us to focus on $VO(acac)_2$ as the catalyst of choice for the conversion of divinyl propargyl alcohols to trienoates. Following optimization, it was found that aromatic hydrocarbon solvents gave the cleanest reactions while elevated temperatures permitted short reaction times (Table 3). Unfortunately, no effective E/Z selectivity was obtained when adducts of unsymmetrically substituted dienones were used. This was not surprising given the similarity in vinyl group substitution.

One limitation of the $VO(acac)_2$-catalyzed protocol is its lack of applicability to the adducts of other acetylides apart from ethoxyacetylene. In these cases, the starting propargyl alcohols underwent decomposition with no evidence for the formation of carbonyl-containing compounds.[12] Therefore, the gold-catalyzed Meyer−Schuster reaction was also attempted on acetylide adducts of dienone **4b** (Scheme 6).[5] With these propargyl alcohols, no Meyer−Schuster products

SCHEME 5. Proposed Catalytic Cycle of Gold-Catalyzed Meyer−Schuster Rearrangement



were observed, but cycloisomerization did occur. Exclusive formation of the dehydrative cyclization product in good to excellent yield was possible when the reaction was carried out in the presence of molecular sieves, giving the corresponding methylene cyclopentenes. A *trans* relationship between the neighboring phenyl substituents was seen in all of these products, confirmed by X-ray diffraction analysis in the case of **10b**. This stereochemical outcome provides support for a Nazarov-type conrotatory cyclization pathway. Akai's modified conditions[13] were also attempted, also giving rise to the methylenecyclopentenes described.

Finally, one other example of unanticipated reactivity was observed under gold catalysis with a propargyl alcohol derived from a different dienone (Scheme 7). Treatment of **4e** under the conditions previously described afforded cyclopentanedione **13e** as the major product, along with lesser

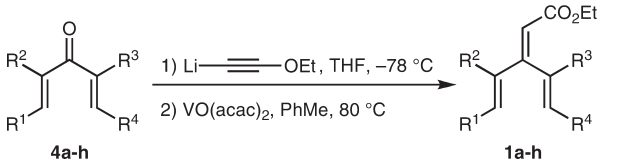
(10) The exocyclic elimination over the expected Saytzeff elimination has also been observed in the tandem Nazarov cyclization/Michael addition of arenes to dienones with bulky β-substituents: Rieder, C. J.; Fradette, R. J.; West, F. G. *Chem Commun*. **2008**, 1572–1574.

(11) In the absence of added water, an intermolecular hydroxylation seems unlikely since trienoate is formed under stringently anhydrous conditions. Additionally, the trienoate is the sole product observed in the crude ^{1}H NMR with no evidence of hydration product **8**.

(12) While the attempted rearrangement of alkynes bearing nonethoxy groups was unsuccessful, it should be noted that the ester provides a convenient functional group for further modification via conversion to the corresponding Weinreb amide and treatment with Grignard reagent. See ref 3 for details.

(13) Egi, M.; Yamaguchi, Y.; Fujiwara, N.; Akai, S. *Org. Lett*. **2008**, *10*, 1867–1870.

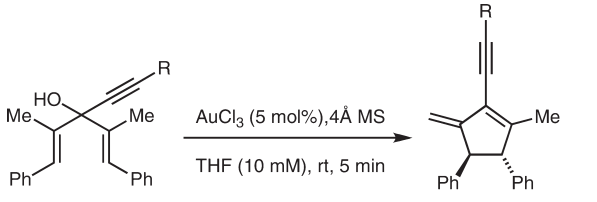
TABLE 3. Meyer–Schuster Homologation of Dienones



					% yield[b]	
dienone[a]	R^1	R^2	R^3	R^4	**3**	**1**
4a	$(CH_2)_3$		$(CH_2)_3$		99	61
4b	Ph	Me	Me	Ph	99	84
4c	*i*-Pr	Me	Me	*i*-Pr	98	76
4d	Ph	Me	Me	H	92	81[c]
4e	$(CH_2)_4$		Me	H	93	80[c]
4f	$(CH_2)_4$		$(CH_2)_4$		96	78
4g	Me	Me	Me	Me	97	75
4h	Ph	H	H	Ph	99	82
4i	4-ClPh	Me	Me	4-ClPh	99	70
4j	4-MeO Ph	Me	Me	4-MeO Ph	98	79

[a]Dienones **4a–g**, alcohols **3a–g**, and trienes **1a–g** are previously described in the Supporting Information for ref 3. [b]All yields indicate isolated product following purification. [c]Unsymmetrical dienones **4d** and **4e** furnished mixtures of geometrical isomers: **1d** (inseparable 1:1 *E*/*Z* mixture) and **1e** (separable 7:3 *E*/*Z* mixture).

SCHEME 6. Gold-Catalyzed Dehydrative Cyclization of Propargyl Alcohols



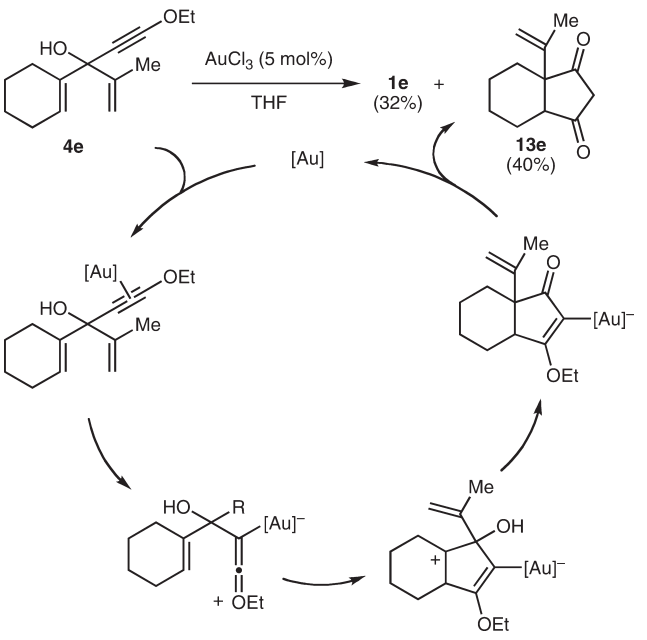
amounts of desired trienoate **1e**.[14] This surprising product is believed to arise from gold activation of the alkyne, followed by formal 5-endo ring closure to give a fused bicyclic intermediate with a bridgehead carbocation. Oxygen-assisted 1,2-shift followed by gold protonolysis and enol ether hydrolysis would then afford the observed product **13e**. Unique observation of this cyclization with **4e** may be the result of unusual conformation preferences, but explanation for the occurrence of this unexpected result requires further study.

Summary

Because of the sensitivity of α,α′-divinylpropargyl alcohols, even under mildly acidic conditions, many of the methods previously reported fail to promote their Meyer–Schuster rearrangement to the corresponding [3]dendralenes, generating a host of byproducts. The use of metal oxides allows for the 1,3-transposition of the alcohol regioselectively across the alkyne functionality, generating cross-conjugated trienoates as a result.

(14) Product **13e** was formed as a single diastereomer, but the relative stereochemistry could not be conclusively assigned based on 2D TROESY data.

SCHEME 7. Unexpected Gold-Catalyzed Cyclization of 4e



On the other hand, catalytic gold(III) chloride appears to effect Brønsted-acid mediated dehydration. The resulting pentadienyl cation then undergoes rapid cyclization, generating alkylidene cyclopentenes. The addition of an amine base prevents the initial dehydration sequence, allowing for alkyne activation by the gold catalyst and generating α,β-unsaturated esters via a possible oxetene intermediate.

Experimental Section

Reactions were carried out in flame-dried glassware under a positive argon atmosphere unless otherwise stated. Transfer of anhydrous solvents and reagents was accomplished with oven-dried syringes or cannulas. Solvents were distilled before use: methylene chloride from calcium hydride; tetrahydrofuran, diethyl ether, and benzene from sodium/benzophenone ketyl; toluene from sodium metal. Thin-layer chromatography was performed on glass plates precoated with 0.25 mm Kieselgel 60 F254. Flash chromatography columns were packed with 230–400 mesh silica gel. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded at 300, 400, or 500 MHz, and coupling constants (*J*) are reported in hertz (Hz). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 100 or 125 MHz.

Typical Procedure for Acetylide Addition[15]**.** ^{n}BuLi (860 μL, 3.1 M, 2.7 mmol) was added to a stirred solution of ethyl ethynyl ether (475 μL, 2.7 mmol) in THF (4.0 mL) at −78 °C. After 30 min, the reaction was allowed to warm to 0 °C and held there for 2 h. The mixture was cooled to −78 °C and dibenzylidene-3-pentanone **4b** (710 mg, 2.7 mmol) in THF (6.0 mL) was added dropwise by cannula forming a white precipitate. After 30 min, the reaction was allowed to warm to 0 °C, which redissolved the precipitate. The reaction was quenched with H_2O (5 mL), and the layers were separated. The aqueous phase was neutralized with 1 M HCl (aq) and was extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with H_2O (5 mL) and brine (5 mL), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (50 g silica, 20:1 hexanes/EtOAc) gave 901 mg (100%) of the desired alcohol **3b** as a viscous orange oil.

(15) References for previously reported dienones **4a–h** and preparative procedures for **4i,j** are found in the Supporting Information.

3-Ethoxyethynyl-1,5-diphenyl-1,4-pentadien-3-ol (3h): yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41−7.44 (m, 4H), 7.29−7.33 (m, 4H), 7.22−7.27 (m, 2H), 6.89 (d, 2H, J = 15.7 Hz), 6.32 (d, 2H, J = 15.7 Hz), 4.21 (q, 2H, J = 7.1 Hz), 1.44 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.5, 132.6, 129.1, 128.6, 127.8, 126.8, 96.3, 75.0, 71.3, 38.9, 14.5; IR (film) ν 3457 (br), 3062, 3030, 2981, 2937, 2903, 2253, 1956, 1890, 1630, 1599, 1584, 1495, 1451 1372 cm^{-1}. Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.68; H, 6.62. Found: C, 82.92; H, 6.81.

3-Ethoxyethynyl-1,5-bis(4-chlorophenyl)-2,4-dimethyl-1,4-pentandien-3-ol (3i): yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (br d, 4H, J = 8.7 Hz), 7.24 (br d, 4H, J = 8.7 Hz), 7.01 (br s, 2H), 4.19 (q, 2H, J = 7.1 Hz), 2.27 (s, 1H), 1.84 (d, 6H, J = 1.3 Hz), 1.43 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.4, 136.3, 132.2, 130.3, 128.3, 125.1, 96.2, 78.3, 74.9, 39.5, 14.5, 13.9; IR (film) ν_{max} 3434 (br), 2982, 2921, 2850, 2262, 1652 (w), 1592 (w), 1490, 1442, 1401 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{22}O_2Cl_2$ (M^+) 400.0997, found 400.0993 (25%), 402.0968 (17%). Anal. Calcd for $C_{23}H_{22}O_2Cl_2$: C, 68.83; H, 5.53. Found: C, 68.82; H, 5.57.

3-Ethoxyethynyl-1,5-bis(4-methoxyphenyl)-2,4-dimethyl-1,4-pentandien-3-ol (3j). Yellow oil; IR (film) ν_{max} 3478 (br), 3031, 2955, 2913, 2835, 2260, 1607, 1574 (w), 1510, 1465, 1442 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, 4H, J = 8.6 Hz), 7.01 (br s, 2H), 6.90 (d, 4H, J = 8.6 Hz), 4.18 (q, 2H, J = 7.1 Hz), 3.38 (s, 6H), 2.29 (s, 1H), 1.87 (d, 6H, J = 1.3 Hz), 1.43 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.2, 137.3, 130.5, 130.3, 125.4, 113.6, 95.9, 78.6, 74.7, 55.3, 40.0, 14.5, 14.0; HRMS (EI) m/z calc'd for $C_{25}H_{28}O_4$ (M^+) 392.1988; found 392.1990 (13%). Anal. Calcd for $C_{25}H_{28}O_4$ C, 76.50; H, 7.19. Found C, 76.35; H, 6.80.

2,4-Dimethyl-1,5-diphenyl-3-phenylethynyl-1,4-pentadien-3-ol (3k): white solid; mp 95−96 °C (uncorr); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53−7.57 (m, 2H), 7.36−7.41 (m, 11H), 7.26−7.31 (m, 2H), 7.22 (q, 2H, J = 1.3 Hz), 2.54 (s, 1H), 2.00 (d, 6H, J = 1.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 137.7, 131.8, 129.1, 128.6, 128.4, 128.2, 126.9, 126.7, 122.6, 89.9, 87.6, 78.8, 13.9; IR (film) ν 3445 (br), 3081, 3056, 3023, 2981, 2953, 2917, 2225, 1599, 1499, 1443 cm^{-1}; HRMS (EI) m/z calc'd for $C_{27}H_{24}O$ (M^+) 364.1827, found 364.1828 (37%). Anal. Calcd for $C_{27}H_{24}O$: C, 88.97; H, 6.64. Found: C, 88.88; H, 6.63.

2-Methyl-3-(1-methyl-2-phenylvinyl)-1-phenylnon-1-en-4-yn-3-ol (3l): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.45 (m, 8H), 7.21−7.26 (m, 2H), 7.10 (br s, 2H), 2.35 (t, 2H, J = 6.9 Hz), 2.22 (d, 1H, J = 1.4 Hz), 1.88 (d, 6H, J = 1.3 Hz), 1.54−1.62 (m, 2H), 1.43−1.53 (m, 2H), 0.95 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 137.8, 129.6, 129.0, 128.4, 128.1, 126.5, 126.3, 88.5, 81.0, 78.4, 30.7, 22.0, 18.6, 13.8, 13.6; IR (film) ν 3456 (br), 3081, 3056, 3023, 2957, 2931, 2872, 2861, 2232, 1622, 1492, 1445 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{28}O$ (M^+) 344.2140, found 344.2135 (2.5%), 326.2040 [$M - H_2O$]$^+$ (100%). Anal. Calcd for $C_{25}H_{28}O$: C, 87.16; H, 8.19. Found: C, 87.21; H, 8.01.

2,4-Dimethyl-1,5-diphenyl-3-(trimethylsilyl)ethynyl-1,4-pentadien-3-ol (3m): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 − 7.39 (m, 8H), 7.22 − 7.27 (m, 2H), 7.11 (br s, 2H), 1.89 (d, 6H, J = 1.2 Hz), 0.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.6, 137.4, 129.0, 128.0, 126.6, 126.5, 105.9, 92.5, 78.4, 13.6, −0.27; IR (film) ν 3549, 3446 (br) 3082, 3057, 3024, 2959, 2919, 2860, 2163, 1600, 1494, 1444, 1381, 1251 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{28}SiO$ (M^+) 360.1910, found 360.1898 (10%), 342.1799 [$M - H_2O$]$^+$ (33%). Anal. Calcd for $C_{24}H_{28}SiO$: C, 79.95; H, 7.83. Found: C, 79.92; H, 7.89.

Typical Procedure for VO(acac)$_2$ Rearrangements. Vanadium oxyacetylacetonate (2 mg, 8 μmol) was added to a stirred solution of dibenzylidene-2-(ethoxyethynyl)-2-propanol **3b** (60 mg, 0.20 mmol) in toluene (2 mL). The reaction was then brought to 80 °C over 1 h and held there for 1 h. The reaction mixture was cooled and filtered through a silica gel plug with diethyl ether (20 mL). The mixture was concentrated and purified through flash chromatography (20:1 hexanes/EtOAc; 5 g silica) to provide 49 mg (82%) of the trienyl ester **1h** as a viscous yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (dd, 1H, J = 16.5, 1.0 Hz), 7.56−7.59 (m, 2H), 7.51−7.53 (m, 2H), 7.29−7.42 (m, 6H), 7.06 (br s, 2H), 7.02 (d, 1H, J = 16.5 Hz), 6.03 (s, 1H), 4.25 (q, 2H, J = 7.1 Hz), 1.35 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 151.3, 136.7, 136.5, 136.3, 135.2, 128.8, 128.7, 128.7, 128.6, 127.3, 127.2, 127.1, 125.2, 115.5, 60.0, 14.4; IR (film) ν 3059, 3026, 2980, 2936, 1702, 1631, 1616, 1580, 1570, 1497, 1448, 1150 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{20}O_2$ (M^+) 304.1463, found 304.1460 (10%). Anal. Calcd for $C_{21}H_{20}O_2$: C, 82.68; H, 6.62. Found: C, 83.06; H, 6.87.

Ethyl 5-(4-chlorophenyl)-3-(1-methyl-2-(4-chlorophenyl)vinyl)-4-methyl-2,4-pentadienoate (1i): colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32−7.38 (m, 6H), 7.22−7.26 (m, 2H), 6.90 (br s, 1H), 6.24 (q, 1H, J = 1.5 Hz), 6.01 (s, 1H), 4.20 (q, 2H, J = 7.1 Hz), 2.13 (d, 3H, J = 1.5 Hz), 2.10 (d, 3H, J = 1.2 Hz), 1.29 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 161.4, 137.0, 136.2, 136.1, 134.1, 133.4, 132.6, 130.9, 130.5, 128.7, 128.6, 127.5, 116.2, 60.3, 19.3, 15.7, 14.6; IR (film) ν 2980, 1716, 1589, 1489 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{22}O_2Cl_2$ (M^+) 400.0997, found 400.1005 (98%), 402.0980 (67%). Anal. Calcd for $C_{23}H_{22}O_2Cl_2$: C, 68.83; H, 5.53. Found: C, 68.69; H, 5.49.

Ethyl 5-(4-methoxyphenyl)-3-(1-methyl-2-(4-methoxyphenyl)-vinyl)-4-methyl-2,4-pentadienoate (1j): colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34−7.38 (m, 2H), 7.26−7.30 (m, 2H), 6.91−6.96 (m, 5H), 623 (br s, 1H), 5.96 (s, 1H), 4.18 (q, 2H, J = 7.2 Hz), 3.85 (s, 3H), 3.85 (s, 3H), 2.14 (d, 3H, J = 1.4 Hz), 2.12 (d, 3H, J = 1.1 Hz), 1.28 (t, 3H, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 162.7, 159.1, 158.5, 135.1, 134.8, 131.2, 130.7, 130.4, 130.3, 128.0, 115.1, 113.9$_2$, 113.9$_0$, 60.2, 55.5, 19.3, 15.8, 14.6; IR (film) ν 2978, 2954, 2836, 1715, 1606, 1586, 1511, 1464 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{28}O_4$ (M^+) 392.1988, found 392.1994 (100%). Anal. Calcd for $C_{25}H_{28}O_4$: C, 76.50; H, 7.19. Found: C, 76.10; H, 7.23.

Typical Procedure for Gold-Catalyzed Reactions. $AuCl_3$ (1.3 mg, 4 μmol) and 4 Å MS (10 mg) were added to a 3 dram vial equipped with a septum. The vial was alternately evacuated and flushed with argon. THF (4.0 mL) was then added and allowed to stand for 15 min. A solution of dibenzylidene-3-(2-phenylethynyl)-3-pentanol **3i** (20 mg, 0.055 mmol) in THF (1 mL) was added via cannula. After 5 min, the reaction mixture was filtered through silica gel (2 g) with Et_2O (25 mL). The filtrate was concentrated and purified by flash chromatography (10 g silica, 20:1 hexanes/EtOAc) to give 19 mg (98%) of dienyne **10b** as a crystalline white solid (mp = 109−110 °C).

1-Methyl-3-methylene-4,5-*trans*-diphenyl-1-cyclopentene-1-acetic acid, ethyl ester (5b): yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.08 (m, 10H), 4.93 (d, 1H, J = 2.1 Hz), 4.55 (m, 1H), 4.20 (q, 2H, J = 7.1 Hz), 3.75 (m, 1H), 3.68 (m, 1H), 3.39 (d, 1H, J_{AB} = 15.8 Hz), 3.36 (d, 1H, J_{AB} = 15.8 Hz), 1.70 (s, 3H), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 157.5, 147.5, 145.6, 143.9, 132.3, 128.6, 128.5, 127.6, 127.6, 126.6, 126.2, 102.2, 64.45, 60.8, 58.4, 31.4, 14.2, 13.9; IR (film) ν 3082, 30631, 3027, 2980, 2930, 1736, 1627, 1601, 1492, 1452, 1171 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{24}O_2$ (M^+) 332.1776, found 332.1778 (100%). Anal. Calcd for $C_{23}H_{24}O$: C, 83.10; H, 7.28. Found: C, 82.77; H, 7.46.

2-Ethoxyethynyl-1-methyl-3-methylene-4,5-*trans*-diphenyl-1-cyclopentene (7b): yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20−7.33 (m, 6H), 7.07−7.14 (m, 4H), 5.22 (d, 1H, J = 2.4 Hz), 4.60 (d, 1H, J = 1.4 Hz), 4.27 (q, 2H, J = 7.1 Hz), 3.81 (m, 1H), 3.74 (m, 1H), 1.81 (d, 3H, J = 1.3 Hz), 1.50 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 145.1, 143.8, 128.9, 128.7, 128.1, 127.9, 126.9, 126.5, 103.9, 75.4, 64.4, 58.7, 33.3, 15.5, 14.7; IR (film) ν 3083, 3061, 3027, 2982, 2927, 2852, 2256, 1634, 1601, 1492, 1452 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{22}O$ (M^+) 314.1670,

found 314.1669 (40%). Anal. Calcd for $C_{23}H_{22}O$: C, 87.86; H, 7.05. Found: C, 87.97; H, 7.27.

1-Methyl-3-methylene-4,5-*trans*-diphenyl-2-phenylethynyl-1-cyclopentene (10b): white solid; mp 109−110 °C (uncorr); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54−7.56 (m, 2H), 7.28−7.38 (m, 7H), 7.21−7.25 (m, 2H), 7.09−7.15 (m, 4H), 5.36 (dq, 1H, J = 2.5, 0.5 Hz), 4.70 (dq, 1H, J = 2.0, 0.5 Hz), 3.87 (m, 1H), 3.80 (m, 1H), 1.92 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 154.9, 144.5, 143.0, 131.7, 131.5, 128.7, 128.6, 128.5, 128.3, 128.3, 128.3, 128.3, 128.2, 128.0, 127.8, 127.7, 126.8, 126.4, 124.1, 123.3, 104.7, 95.3, 82.8, 64.6, 58.5, 15.6; IR (film) ν 3081, 3060, 3027, 2969, 2929, 2905, 2206, 1600, 1491, 1452 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{22}$ (M^+) 346.1721, found 346.1716 (45%). Anal. Calcd for $C_{27}H_{22}$: C, 93.60; H, 6.40. Found: C, 93.41; H, 6.41.

2,4-Dimethyl-1,5-diphenyl-3-phenylethynyl-1,3-cyclopentadiene (*endo*-10b). Upon standing in the presence of trace acid or chromatography on untreated silica gel, **10b** underwent double-bond isomerization into the ring to give varying mixtures of **10b** and the corresponding alkynylcyclopentadiene ***endo*-10b**: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07−7.56 (m, 15H), 4.45 (q, 1H, J = 1.9 Hz), 2.30 (d, 3H, J = 1.9 Hz), 2.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 142.1, 138.3, 137.1, 136.3, 131.5, 128.6, 128.4, 128.3, 128.3, 128.2, 128.0, 126.5, 126.0, 125.3, 123.6, 94.5, 84.4, 63.0, 14.4, 13.5; IR (film) ν 3080, 3060, 3027, 2967, 2928, 2871, 2192, 1599, 1491, 1451 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{22}$ (M^+) 346.1721, found 346.1719; Anal. Calcd for $C_{27}H_{22}$: C, 93.60; H, 6.40. Found: C, 93.96; H, 6.55.

1-Methyl-3-methylene-4,5-*trans*-diphenyl-2-(1-hexynyl)-1-cyclopentene (11b): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05−7.33 (m, 10H), 5.25 (dq, 1H, J = 2.5, 0.7 Hz), 4.26 (dq, 1H, J = 2.0, 0.7 Hz), 3.81 (m, 1H), 3.74 (m, 1H), 2.50 (t, 2H, J = 7.0 Hz), 1.83 (d, 3H, J = 1.5 Hz), 1.48−1.69 (m, 4H), 0.98 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 153.3, 145.0, 143.5, 128.9, 128.7, 128.5, 128.4, 128.2, 127.9, 126.9, 126.7, 126.6, 104.4, 96.7, 74.0, 64.6, 58.7, 31.3, 22.2, 19.5, 15.6, 13.9; IR (film) ν 3085, 3061, 3029, 2959, 2932, 2872, 2215, 1681, 1601, 1495, 1452 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{26}$ (M^+) 326.2035, found 326.2032 (15%). Anal. Calcd for $C_{25}H_{26}$: C, 91.97; H, 8.03. Found C, 91.80; H, 8.16.

1-Methyl-3-methylene-4,5-*trans*-diphenyl-2-(trimethylsilyl)-ethynyl-1-cyclopentene (12b). Compound **12b** partially isomerizes to its corresponding *endo*-isomer during the necessary time frame of ^{13}C NMR spectral acquisition: white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20−7.32 (m, 6H), 7.10−7.12 (m, 2H), 7.05−7.08 (m, 2H), 5.27 (dq, 1H, J = 2.5, 0.6 Hz), 4.66 (dq, 1H, J = 2.1, 0.6 Hz), 3.82 (m, 1H), 3.75 (m, 1H), 1.886 (app dt, 3H, J = 1.6, 0.6 Hz), 0.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 155.3, 144.4, 142.9, 128.7, 128.5, 127.8, 127.7, 126.8, 126.4, 104.7, 100.6, 64.5, 58.5, 15.6, 0.2; IR (film) ν 3083, 3061, 3027, 2961, 2926, 2854, 2149, 1636, 1600, 1494, 1452, 1261 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{26}Si$ (M^+) 342.1804, found 342.1803 (78%). Anal. Calcd for $C_{24}H_{26}Si$: C, 84.15; H, 7.75. Found: C, 84.30; H, 7.80.

4-Isopropenylhexahydro-1,3-indandione (13e): colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.94 (m, 1H), 5.82 (m, 1H), 3.75 (m, 1H), 3.39 (dd, 1H, J = 15.6, 2.2 Hz), 2.92 (dd, 1H, J = 15.6, 1.4 Hz), 2.56 (m, 1H), 2.10 (m, 1H), 1.96 (dd, 3H, J = 1.5, 0.9 Hz), 1.64 (m, 2H), 1.58 (m, 2H), 1.24 (m, 1H), 1.11 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.4, 203.8, 140.3, 126.0, 60.0, 58.2, 41.6, 34.2, 22.2, 21.3, 20.7, 18.6; IR (film) ν 2932, 2858, 1780, 1664, 1448 cm^{-1}; HRMS (EI) m/z calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150, found 192.1151.

Hydration of 3b with $GaCl_3$. $GaCl_3$ (5 mg, 28 μmol) was added to a 5 mL round-bottom flask and alternatively evacuated and flushed with argon. (N.B. During weighing and transfer, the white/gray solid $GaCl_3$ begins to smoke, and portions melt into a black liquid.) To this was added THF (1 mL) and the mixture cooled to −40 °C. To this was added **3b** (9.5 mg, 29 μmol) in THF (1 mL) and the mixture immediately brought to room temperature. After 1 h, the reaction was treated with saturated aqueous $NaHCO_3$ (1 mL) and extracted with Et_2O (3 × 3 mL). The combined organic phases were dried over $MgSO_4$, concentrated, and purified with PTLC (10:1 hexanes/EtOAc) to give **1b** (2.7 mg, 28%) and **8b** (4.4 mg, 46%):

Ethyl 3-hydroxy-4-methyl-3-(1-methyl-2-phenylvinyl)-5-phenyl-4-pentenoate (8b): colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20−7.36 (m, 10H), 6.70 (s, 2H), 4.75 (s, 1H), 4.21 (q, 2H, J = 7.1 Hz), 3.02 (s, 2H), 1.84 (d, 6H, J = 1.3 Hz), 1.27 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 139.5, 137.9, 129.0, 128.2, 128.1, 126.4, 125.7, 79.5, 61.1, 41.4, 14.1; IR (film) ν 3470 (br), 3057, 3023, 2958, 2927, 2857, 1719, 1599, 1492, 1445, 1370, 1195, 1162 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{24}O_2$ [M − H_2O]$^+$ 331.1776, found 331.1779 (100%).

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Supporting Information Available: Experimental procedures for **4i**,**j**; ^{1}H and ^{13}C NMR spectra for **1h**−**j**, **3i**−**m**, **4i**,**j**, **5b**, **7b**, **8b**, **10b**, ***endo*-10b**, **11b**, **12b**, and **13e**; and ORTEP structure and X-ray data for **10b**. This material is available free of charge via the Internet at http://pubs.acs.org.