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Torquoselectivity in the Nazarov Reactions of Allenyl Vinyl Ketones

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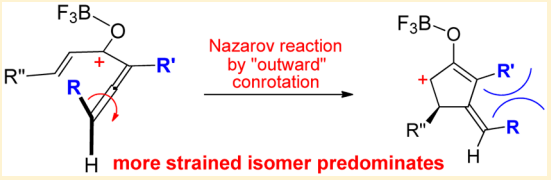
Supporting Information

ABSTRACT: Nazarov reactions mediated by BF_3-etherate of a series of carbon-substituted allenyl vinyl ketones provided intermediates in which substituents on the termini of the allenes had rotated away from the vinyl moieties, and these intermediates were trapped by (4 + 3)-cyclizations. A computational examination of the torquoselectivity of these Nazarov reactions confirmed a kinetic preference for the observed isomers and pointed to steric interactions and the degree of allene deformation as significant factors in determining the torquoselectivity. The study also suggested that the high proportion of one geometrical isomer in the Nazarov products might also be due to some preferential trapping of the major Nazarov intermediate.

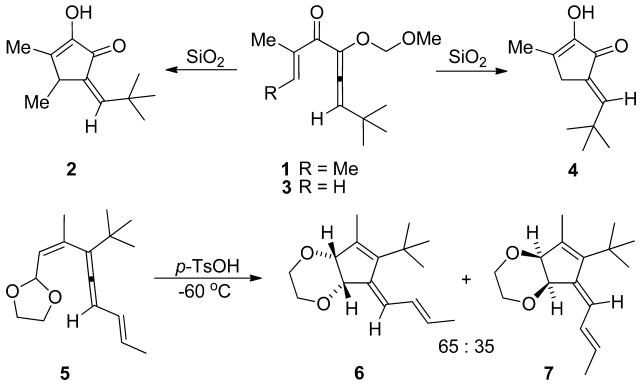


INTRODUCTION

The Nazarov reaction is a conrotatory 4π-electrocyclization that is mediated by an acid.[1,2] With appropriately substituted divinyl ketones, different senses of rotation, clockwise and anticlockwise, lead to products that differ in the chirality of the newly formed tetrahedral center(s). A bias in the sense of rotation, i.e., the torquoselectivity, can be been observed in instances where the substrate is chiral or when the reaction is mediated by a chiral acid.[3,4] Torquoselectivity with an allenyl vinyl ketone (AVK) in which the allene has axial chirality provides products that differ in the *E*/*Z*-geometries of their alkenes,[5] and so the degree of torquoselectivity of a Nazarov reaction of an AVK can be assessed, even with a racemic substrate, by observing the ratio of the double-bond isomers in the product.

Tius and co-workers[5−9] have provided a large body of work on the Nazarov reactions of AVKs substituted on the allene by an oxygen function. With such a substrate the oxyallyl cation intermediate collapses to a ketone product by the loss of the group on the allenic oxygen. When the terminus of the allene is substituted, there is a general preference for the formation of the exocyclic alkene with the *Z*-geometry. Reactions of enantiomerically enriched substrates with axially chiral allenes provided products of predominantly one double-bond geometry and with enriched point chirality on the adjacent tetrahedral carbon.[6,7] Although the control of torquoselectivity in 4π-electrocyclic processes has been ascribed to orbital interactions,[10−12] Tius provided a steric rationale for the torquoselectivity in the Nazarov reactions of his AVKs in which the conrotatory cyclization rotated the larger group on the terminus of the allene away from the alkene moiety.[8] The Nazarov reaction of AVK **1** giving **2** is representative of a number of reactions reported by Tius that provided kinetic products with a high degree of torquoselectivity (Scheme 1).[9] Equilibration of the kinetic products to the opposite geometric isomers was facile in many instances.[8] However, AVK **3**, with an alkene moiety having no terminal substitution, cyclized to yield the *E*-product **4** as the kinetic product. In this instance conrotation appeared to take place in the sense that avoided an unfavorable interaction between the *tert*-butyl group and the oxygen function.[9]

Scheme 1. Torquoselective Nazarov Reactions of AVKs 1 and 3[9] and the 4π-Electrocyclization of 5[13]



In related chemistry, the carbocation generated by protonation of the acetal **5** underwent 4π-electrocyclization with little torquoselectivity, and the resulting isomeric cationic intermediates were trapped intramolecularly as the 1,4-dioxins **6** and **7** (Scheme 1).[13] Other substituents on the terminus of the allene resulted in different torquoselectivities. The products from this study underwent isomerization of the exocyclic double bond under the reaction conditions.

Nazarov reactions of hydrocarbon-substituted AVKs such as **8** are efficiently mediated by BF_3-etherate, and the cationic intermediate **9** can be intercepted in a number of ways,[14,15] including by (4 + 3)-cyclization with acyclic dienes to give a bicyclic product such as **10** (Scheme 2).[16,17]

Presented here are the results of an investigation of torquoselectivity of Nazarov reactions of carbon-substituted AVKs based on **8**. Carbon substitution allows for structural

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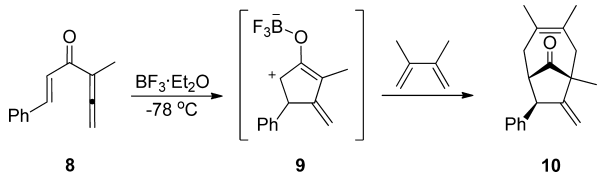
Scheme 2. Nazarov Reaction of AVK 8 with Interception of the Cationic Intermediate 9 by a (4 + 3)-Cyclization[16]

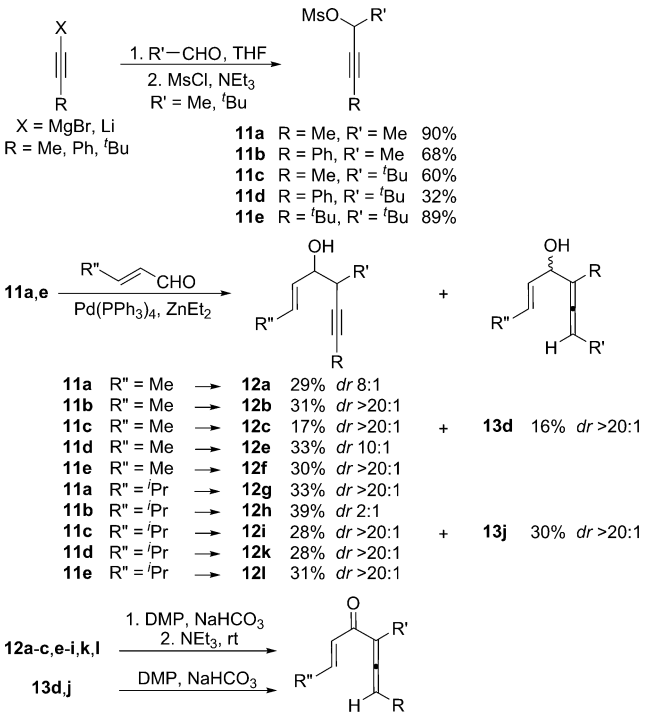


variation at a number of positions, and the opportunity to intercept the cationic intermediate by (4 + 3)-cyclization should lead to products that would not be prone to isomerize under the reaction conditions. Our results provide important information regarding the nature of the control of torquoselectivity.

RESULTS AND DISCUSSION

Preparation of AVKs. Twelve substituted AVKs **14a–l** were obtained in racemic form in sufficient amounts for study in the manner outlined in Scheme 3. Addition of

Scheme 3. Preparation of AVKs (±)-14a–l



alkynylmagnesium or alkynyllithium reagents to two aldehydes gave known alcohols that were converted to mesylates **11**.[18] These were not rigorously purified due to their limited stability. Following the procedure of Marshall and Adams[19] the organozinc reagents derived from these crude mesylates were reacted with two unsaturated aldehydes to provide ten enyne-alcohols **12**. The reactions involving hindered mesylate **11c** gave mixtures of S_N2 and S_N2' products, the latter products being the allenes **13d** and **13j**. This lack of selectivity was exploited to give AVKs **14d** and **14j**. It appeared that the yields by this organozinc method were lowered by competitive reactions involving the conjugated double-bond, and when acrolein itself was employed as a substrate the yields of the desired alcohols were zero. (Thus, AVKs with R″ = H were not available for study.) Oxidation of the alcohols with Dess–Martin periodinane in the presence of $NaHCO_3$[20] followed by isomerization of the alkynes to allenes with NEt_3 provided the AVKs. The alkyne–allene isomerization was not favorable in some instances, e.g., **14a**, but the reason is not known.

Nazarov Reactions Followed by (4 + 3)-Cyclizations. In the conrotatory Nazarov reactions of AKVs **14a–l**, the sense of rotation should determine the geometry of the exocyclic double-bond (Figure 1). The sense of rotation in which the

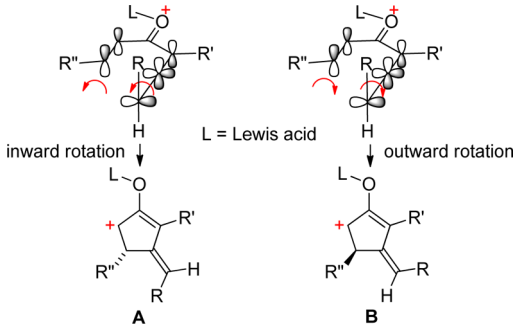


Figure 1. Torquoselectivity with a substituted AVK.

substituent R on the terminus of the allene moves toward the alkene moiety, herein called "inward" rotation, leads to the cyclic oxyallyl cation intermediate **A**. In **A**, R is close to R″, the substituent that was on the terminus of the *E*-alkene. Rotation in the other sense, herein called "outward" rotation, gives intermediate **B**, which has R close to R′, a substituent that was on the allene α to the carbonyl.

A solution of each AVK in dichloromethane at −78 °C was treated for 5 to 10 min with one equivalent of BF_3-etherate and an excess of 2,3-dimethylbutadiene, which trapped the oxyallyl cation intermediate(s) (**A** or **B**) by (4 + 3)-cyclization(s). The results of the tandem Nazarov/(4 + 3)-cyclization processes are summarized in Table 1. No products of simple, untrapped Nazarov reactions were detected. AVK **14a** gave a mixture of isomeric products **15a** and **16a**, in a ratio of 74:26. In contrast, the diastereomeric ratios of the products from all of the other AVKs were at least 20:1 as indicated by integration of the ^1H NMR spectra. Nuclear Overhauser enhancements (NOE) showed that the major, or exclusive, product (**15a–e,g–k**) was the one for which an outward rotation during the Nazarov reaction had placed R and R′ in proximity, i.e., via intermediate **B**, and the (4 + 3)-cyclization had taken place onto the oxyallyl cation intermediate on the face opposite the R″ group. The minor isomer **16a** from **14a** proved by NOE to be the result of inward rotation during the Nazarov reaction, i.e., via intermediate **A**, and not due to the opposite facial selectivity in the (4 + 3)-cyclization; i.e., the diene did not add *syn* to the R″ group.

Terminal substitution of the allene significantly reduced the yields of the Nazarov reactions since the yields of all of these reactions were inferior to the yield with **8**. The largest substituent (R = ^{t}Bu) had the greatest inhibitory effect. AVKs **14b–l** all possess one or more hydrocarbon substituents that should be more sterically demanding than the three methyl substituents on AVK **14a**. The effect of an increase in the size

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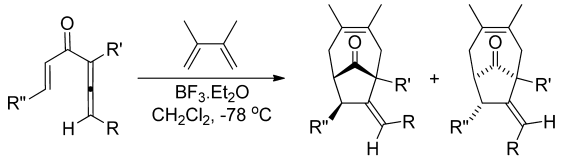
Table 1. Bicyclic Products (±)-15a–k and (±)-16a of the tandem Nazarov/(4 + 3)-Cyclization of AVKs (±)-14a–l in the Presence of 2,3-Dimethylbutadiene



14a-l 15a-l 16a-l

	product(s)				
AVK		R	R′	R″	yield[a] (%)
14a	**15a** + **16a** (74:26)	Me	Me	Me	66
14b	**15b**	Ph	Me	Me	65
14c	**15c**	Me	^{t}Bu	Me	47
14d	**15d**	^{t}Bu	Me	Me	49
14e	**15e**	Ph	^{t}Bu	Me	56
14f	**15f**	^{t}Bu	^{t}Bu	Me	0
14g	**15g**	Me	Me	^{i}Pr	71
14h	**15h**	Ph	Me	^{i}Pr	49
14i	**15i**	Me	^{t}Bu	^{i}Pr	59
14j	**15j**	^{t}Bu	Me	^{i}Pr	36
14k	**15k**	Ph	^{t}Bu	^{i}Pr	77
14l	**15l**	^{t}Bu	^{t}Bu	^{i}Pr	0

[a]Isolated yields following purification by chromatography.

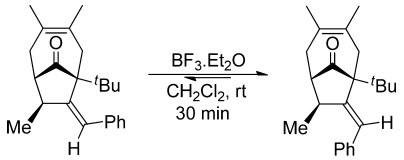
of any substituent was an increase in the proportion of the outward-rotation product. Comparison of the reactions of AVKs **14a** and **14g** showed that increasing the size of substituent R″ enhanced the torquoselectivity, even though the *E*-geometry of the alkene would have had R″ pointing away from the allene moiety in the starting compounds. Nevertheless, both of these factors are in accord with the idea that an outward rotation of the allene minimizes the steric interaction between the termini of the allene and the alkene.

On the other hand, an outward rotation that would lead to the cyclic oxyallyl cation **B** would bring substituent R closer to, and ultimately coplanar with, substituent R′. It might therefore be expected that the torquoselectivity in favor of outward rotation would be reduced by increasing the size of R′. *The opposite was true*, as a comparison of the reactions of AVKs **14a** and **14c** revealed. Even when the sizes of R and R′ were both increased significantly, as with AVKs **14e** and **14k**, the selectivity was still very much in favor of the outward-rotation products. It was hoped that ^{t}Bu-^{t}Bu interactions in intermediate **B** derived from **14f** and **14l** would lead to the isolation of some products derived from **A**. Instead, no trapped Nazarov products were obtained from the attempted Nazarov reactions with these AVKs.

In order to confirm that the isolated products had not equilibrated under the reaction conditions, compounds **15c** and **15e** were reintroduced to a solution of BF_3-etherate in dichloromethane, but at room temperature. After 30 min the phenyl-substituted product **15e** had equilibrated to a 80:20 mixture of **16e** and **15e** (Scheme 4) but the alkyl-substituted product **15c** remained unchanged.

Computational Results. The Nazarov reactions of AVKs **14a–l** were examined computationally using the dispersion-corrected ωB97X-D functional[21] with the 6-31+G(d,p) basis set. Some salient features from these calculations are summarized in Table 2. In every instance, the more stable product from the Nazarov reaction was the result of inward

Scheme 4. Equilibration of Compound (±)-15e to (±)-16e



15e 16e

rotation, cation **A**. It was surprising that the AVKs with R = phenyl, i.e., AVKs **14b** and **14h**, had transition state energies leading to **A** and to **B** that were almost equal, but the transition state energies leading to cation **B** were lower than to **A** with all the other AVKs.

There were consistent geometrical differences between the transition states leading to **A** and to **B**. The incipient five-membered ring is not planar at the transition state.[12] Inward rotation to **A** progressed through a geometry in which the alkene was "above" the allene, as depicted in Figure 2. The dihedral $\theta_{\alpha,\beta,\delta,\varepsilon}$ was approximately 25.4°, and the closest contact (presumably the most important steric interaction) across the termini was between an atom of R and H_α. The average distance in our data between these atoms was 2.4 Å. The corresponding steric interaction in the outward transition states to **B** would have been smaller. This is because the transition state for outward rotation to **B** had the alkene "below" the allene, the dihedral $\theta_{\alpha,\beta,\delta,\varepsilon}$ was invariably larger (approximately 28.3°), and the closest contact was between H_α and H_ζ. The average distance, in our data, between these hydrogens was 2.8 Å. On the other hand, outward rotation to **B** could have led to an increase in the steric interaction between R and R′, but at the transition state leading to **B** the closest atoms of R and R′ were still far apart, varying from 3.969 Å for **14a** to 5.002 Å for **14k**. Thus, steric interactions between R and R′ could only play a minor role in the kinetically controlled product distribution. However, the size of R′ did seem to influence the torquoselectivity. This might have been related to the amount by which the allene had bent at the transition state. The unfavored inward rotation transition states were always more bent (ca. 148.0°) than were the outward rotation transition states (ca. 153.5°). Furthermore, the degree of rotation of the allene, dihedral $\theta_{R,\varepsilon,\delta,\gamma}$, was always much more in the transition states for inward rotation (Table 2). The largest differences in transition state energies occurred when the differences in the degree of allene rotation at the transition state were largest, such as for AVKs **14d**, **14f**, **14j** and **14l**. In contrast, differences in the extent of alkene rotation for the two transition states were less than 2°, although the amount of rotation in the transition state for **A** was never larger than the rotation in the transition state for **B**. A reason that products from AVKs **14f** and **14l** were not obtained experimentally might have been because the Nazarov reactions of these by outward rotation to **B** were endothermic by 30.8 and 27.2 kJ·mol^{-1}, respectively, which likely reflected the considerable steric crowding between the two *tert*-butyl groups.

While the calculations confirmed that the products were not the result of thermodynamic control in the Nazarov reactions of the AVKs, the differences in the transition state energies between the inward and outward rotation reactions did not reflect the experimental product ratios accurately. Only AVK **14a** led, after trapping the oxyallyl cations with a diene, to a small ratio of tandem Nazarov/(4 + 3)-products (**15a** and **16a**), but the calculations predicted that small ratios should have

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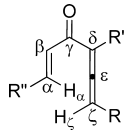
Table 2. Computed (ωB97X-D/6-31+G(d,p) with ZPE Correction) Relative Product and Transition State Energies and Selected Geometrical Data for the Nazarov Transition States of AVKs 14a–l



			closest contact of termini		$\theta_{R,\varepsilon,\delta,\gamma}$ [a]	
AVK	ΔE_{A-B} (kJ·mol^{-1})	$\Delta E_{A-B}^{\ddagger}$ (kJ·mol^{-1})	**A**[b] (Å)	**B**[c] (Å)	**A** (degree)	**B** (degree)
14a	−11.6	4.5	2.573	2.849	142.7	130.7
14b	−13.0	1.3	2.312	2.829	140.6	130.4
14c	−26.0	6.4	2.557	2.839	142.1	127.7
14d	−19.7	20.0	2.261	2.806	160.4	129.3
14e	−13.5	4.1	2.316	2.802	140.3	127.4
14f	−35.5	19.9	2..260	2.758	160.0	123.9
14g	−10.8	3.9	2.614	2.850	143.2	129.2
14h	−12.9	−0.8	2.370	2.831	138.9	127.6
14i	−31.5	6.5	2.594	2.837	143.8	126.8
14j	−20.1	19.5	2.278	2.815	159.8	129.3
14k	−18.0	2.2	2.365	2.803	139.0	125.6
14l	−41.5	17.5	2.278	2.769	160.2	125.8

[a]This dihedral is a measure of the rotation of the allene. [b]The closest contact is between H_α and an atom of R. [c]The closest contact is between H_α and H_ζ.

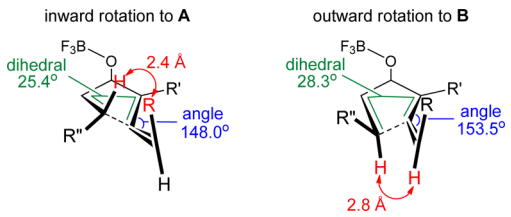
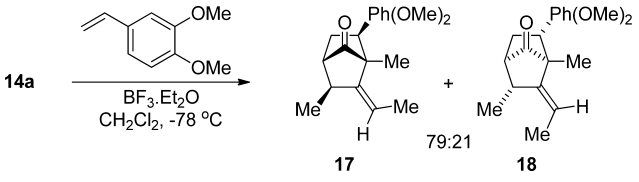


Figure 2. Comparison of the geometries of the Nazarov transition states for inward and outward rotation.

been observed with some other AVKs, such as with **14b** and **14h**. This suggested that the (4 + 3)-trapping reactions were more efficient with **B** than with **A**, and the proportion of products from **B** were enhanced by the trapping reaction.

Nazarov Reaction Followed by (3 + 2)-Cyclization. If the trapping reaction is important in determining the product distribution, then a different mode of trapping might lead to a different ratio of products. In order to test this question, the Nazarov reaction of **14a** was carried out in the presence of 3,4-dimethoxystyrene (Scheme 5). In this instance, the oxyallyl cation intermediates were expected to be trapped by a highly regioselective (3 + 2)-cyclization.[16,22] The product from **14a** was a mixture of the isomeric products **17** and **18** in a ratio of 79:21, respectively,[23] favoring the product from outward rotation: NOE measurements indicated proximity between the methyl on the exocyclic double-bond and the bridgehead methyl for **17**. The ratio of isomers was similar to when the Nazarov reaction of **14a** was intercepted by (4 + 3)-cyclization to give **15a** and **16a**. Thus, the mode of trapping is either not important or (4 + 3)- and (3 + 2)-cyclizations are similarly biased in terms of the rates of cyclization with intermediates **A** and **B**.

Scheme 5. Nazarov Reaction of AVK (±)-14a in the Presence of 3,4-Dimethoxystyrene Giving (±)-17 and (±)-18



CONCLUSIONS

The kinetically favored, but thermodynamically disfavored, product is obtained from the Nazarov reaction of an allenyl vinyl ketone bearing substitution on the terminus of the allene. This is the result of a conrotatory reaction with outward rotation, i.e., in which the terminal substituent on the allene turns away from the alkene moiety. Calculations are consistent with the torquoselectivity being due to steric interactions between substituents on the termini of the alkene and allene moieties. However, a significant secondary factor appears to be the amount of deformation of the allene at the transition state. Outward rotation of the substituent on the terminus of the allene is accompanied by less deformation. Where the calculations predict modest torquoselectivity, more facile trapping of the cationic intermediate **B** by (4 + 3)-cyclization with a diene might result in the isolation very predominantly of a single isomer. This tandem torquoselectective Nazarov/(4 + 3)-cyclization approach provides products in which the double-bond geometry would otherwise be problematic synthetically. Synthetic exploitation is currently under study in our laboratory, and the torquoselectivity of Nazarov reactions with other substrates is presently the subject of a thorough computational study.

EXPERIMENTAL SECTION

General Considerations. Reactions were carried out in oven-dried glassware under an atmosphere of dry nitrogen. Reagents were used as received from commercial sources, except BF_3·OEt_2 was freshly distilled. Dichloromethane was distilled over calcium hydride. Tetrahydrofuran (THF) was freshly distilled over sodium/benzophenone. Reactions were followed by TLC analysis using precoated (silica

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J. Org. Chem. 2015, 80, 1042–1051

gel 60 F254, 0.25 mm) plates with aluminum backing. Column chromatography was carried out with silica gel (40−63 μm particle size, 230−240 mesh). Evaporation of solvents was under reduced pressure with modest heating. Melting points were uncorrected. IR spectra were recorded on an FT instrument on NaCl or CsI plates as neat liquid films, and only significant absorption bands (in cm^{-1}) are reported. ^1H NMR spectra were acquired at 500.1 MHz, and chemical shifts are relative to internal TMS (δ 0.00 ppm). The ^1H NMR data are presented as follows: chemical shift (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant(s), J, in hertz (Hz), and integration. Diastereomeric ratios were determined by integration of clearly separated ^1H NMR signals. ^{13}C NMR spectra were acquired at 125.8 MHz, and chemical shifts are relative to the solvent signal ($CDCl_3$, δ 77.16 ppm). Structural assignments were based on DEPT, 2-D NMR spectra (COSY, HSQC, HMBC) and nuclear Overhauser effect (NOE) measurements.[24] Important NOE contacts are illustrated in the Supporting Information. HRMS data were obtained on a TOF mass spectrometer by positive-ion ESI.

Preparation of Propargyl Alcohols. A solution of 1-propynylmagnesium bromide [0.5 M/THF] or phenylethynylmagnesium bromide [1.0 M/THF] (1 equiv) in THF was cooled to 0 °C. Acetaldehyde or 2,2-dimethylpropanal (1 equiv) was added slowly, and the mixture was stirred and warmed to rt over 2 h. The reaction was quenched by the addition of a saturated solution of NH_4Cl, and the phases were separated. The aqueous phase was extracted with Et_2O (×3). The combined organic layers were washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by chromatography.

3-Pentyn-2-ol. 1-Propynylmagnesium bromide solution (40 mL) with acetaldehyde (1.10 mL); chromatography 40% Et_2O/pentane; yield 1.6 g (95%): liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 4.51−4.48 (m, 1H), 1.84 (d, J = 2.1 Hz, 3H), 1.84 (overlapped, 1H), 1.43 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.6, 80.3, 58.7, 24.8, 3.6. NMR data are consistent with the literature.[25]

4-Phenyl-3-butyn-2-ol. Phenylethynylmagnesium bromide solution (20 mL) with acetaldehyde (1.10 mL); chromatography 40% Et_2O/pentane; yield 2.11 g (72%): liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43−7.41 (m, 2H), 7.30−7.27 (m, 3H), 4.78−4.73 (m, 1H), 2.84 (d, J = 4.9 Hz, 1H), 1.54 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.7, 128.4, 128.3, 122.7, 91.2, 83.9, 58.7, 24.4; HRMS (ESI) 169.0626, $[C_{10}H_{10}ONa]^+$ requires 169.0624. NMR data are consistent with the literature.[26]

2,2-Dimethyl-4-hexyn-3-ol. 1-Propynylmagnesium bromide solution (50 mL) with 2,2-dimethylpropanal (2.80 mL); chromatography 20% Et_2O/pentane; yield 2.19 g (67%): liquid; ^1H NMR (500 MHz, $CDCl_3$) δ 3.98 (q, J = 2.1 Hz, 1H), 1.86 (d, J = 2.2 Hz, 3H), 1.64 (broad s, 1H), 0.98 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 81.8, 79.0, 71.8, 36.0, 25.4, 3.7; HRMS (ESI) 149.0941, $[C_8H_{14}ONa]^+$ requires 149.0937.

4,4-Dimethyl-1-phenylpentyn-3-ol. Phenylethynylmagnesium bromide solution (15 mL) with 2,2-dimethylpropanal (1.60 mL); chromatography 20% Et_2O/pentane; yield 1.23 g (43%): solid; mp 44−46 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.38 (m, 2H), 7.28−7.25 (m, 3H), 4.19 (d, J = 6.1 Hz, 1H), 1.81 (d, J = 6.2 Hz, 1H), 1.02 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.8, 128.5, 128.4, 122.9, 89.1, 85.8, 72.0, 36.3, 25.5; HRMS (ESI) 211.1095, $[C_{13}H_{16}ONa]^+$ requires 211.1093. NMR data are consistent with the literature.[26]

2,2,6,6-Tetramethyl-4-heptyn-3-ol. A solution of 3,3-dimethyl-1-butyne (2.50 mL, 20 mmol) in THF (25 mL) was cooled to −78 °C. MeLi (19 mL of a 1.6 M solution in Et_2O, 30 mmol) was added by syringe pump over 10 min. After 1 h at −78 °C, 2,2-dimethylpropanal (4.30 mL, 40 mmol) was added dropwise. The temperature was maintained at −78 °C for a further 1 h, and then the reaction mixture was warmed to rt over 2 h. The mixture was cooled to 0 °C before the reaction was quenched by the slow addition of H_2O. The phases were separated and the organic phase was washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by chromatography (40% Et_2O/pentane) to provide the title compound (3.00 g, 90%) as a solid: mp 34−36 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 3.97 (d, J = 6.1 Hz, 1H), 1.63 (d, J = 6.1 Hz, 1H), 1.22 (s, 9H), 0.97 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 94.6, 78.4, 71.6, 36.0, 31.2, 27.5, 25.4; HRMS (ESI) 191.1401, $[C_{11}H_{20}ONa]^+$ requires 191.1406. NMR data are consistent with the literature.[27]

Preparation of Propargyl Mesylates. On the basis of a literature procedure,[18] a solution of the propargyl alcohol (1 equiv) in CH_2Cl_2 was cooled to 0 °C. NEt_3 (1.1 equiv) was added followed by the slow addition of MsCl (1.1 equiv). The reaction mixture was warmed slowly to rt over 1 h. A saturated solution of NH_4Cl was added, and the biphasic mixture was stirred for 30 min. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (×3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. Because of their limited stability, the crude mesylates were used without purification within 24 h of their preparation. For 3-pentyn-2-yl methanesulfonate (**11a**): 3-pentyn-2-ol (691 mg) with NEt_3 (1.25 mL) and MsCl (0.68 mL) in CH_2Cl_2 (10 mL) yielded **11a** (1.26 g, 95%) as an oil. For 4-phenyl-3-butyn-2-yl methanesulfonate (**11b**): 4-phenyl-3-butyn-2-ol (1.34 g) with NEt_3 (0.85 mL) and MsCl (0.46 mL) in CH_2Cl_2 (10 mL) yielded **11b** (1.17 g, 95%) as an oil. For 2,2-dimethyl-4-hexyn-3-yl methanesulfonate (**11c**): 2,2-dimethyl-4-hexyn-3-ol (763 mg) with NEt_3 (1.30 mL) and MsCl (0.46 mL) in CH_2Cl_2 (10 mL) yielded **11c** (1.10 g, 89%) as an oil. For 4,4-dimethyl-1-phenylpentyn-3-yl methanesulfonate (**11d**): 4,4-dimethyl-1-phenylpentyn-3-ol (1.06 g) with NEt_3 (1.40 mL) and MsCl (0.78 mL) in CH_2Cl_2 (20 mL) yielded **11d** (1.10 g, 75%) as a dark orange oil. For 2,2,6,6-tetramethyl-4-heptyn-3-yl methanesulfonate (**11e**): 2,2,6,6-tetramethyl-4-heptyn-3-ol (1.03 g) with NEt_3 (1.25 mL) and MsCl (0.70 mL) in CH_2Cl_2 (20 mL) yielded **11e** (1.57 g, 99%) as an off-white solid.

Preparation of (Alkynylmethyl) Vinyl Alcohols. (Alkynylmethyl) vinyl alcohols were synthesized using a procedure based on literature precedent.[19,28,29] $Pd(PPh_3)_4$ (5 mol %) was dissolved in THF (sufficient to make a 0.2 M solution). Mesylate (1 equiv) was added dropwise followed by the aldehyde (1.3 equiv). The mixture was then cooled to 0 °C, and $ZnEt_2$ (1 M solution in hexane, 2.0 equiv) was added via a syringe pump over 40 min. The reaction mixture was stirred as it warmed to rt over 2 h. The reaction was then quenched with 1 M HCl. A saturated solution of NH_4Cl was added, and the phases were separated. The aqueous phase was extracted with Et_2O (×3). The combined organic layers were washed with a saturated solution of NaCl, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography.

*(E)-5-Methyloct-2-en-6-yn-4-ol (**12a**).* Mesylate **11a** (417 mg) and crotonaldehyde (0.30 mL) with $Pd(PPh_3)_4$ (120 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (20% Et_2O/pentane) yielded an inseparable mixture (*dr* 8:1 by ^1H NMR) of diastereomeric alcohols **12a** (103 mg, 29%) as an oil: IR (film) 3413 cm^{-1}; NMR signals for the major diastereomer, ^1H NMR (500 MHz, $CDCl_3$) δ 5.68 (dqd, J = 15.3, 6.5, 0.9 Hz, 1H), 5.43 (ddq, J = 15.3, 7.4, 1.6 Hz, 1H), 3.76 (ddd, J = 7.4, 6.5, 4.4 Hz, 1H), 2.42 (qdq, J = 7.0, 6.5, 2.4 Hz, 1H), 2.07 (d, J = 4.4 Hz, 1H), 1.78 (d, J = 2.4 Hz, 3H), 1.67 (dd, J = 6.5, 1.6 Hz, 3H), 1.07 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.6, 129.1, 80.1, 78.9, 76.3, 33.9, 17.9, 17.7, 3.7; NMR signals discerned for the minor diastereomer, ^1H NMR (500 MHz, $CDCl_3$) δ 5.54 (ddq, J = 15.3, 7.2, 1.6 Hz, 1H), 3.91−3.88 (m, 1H), 2.62−2.57 (m, 1H), 1.03 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 75.6, 33.2, 16.7, 1.7; HRMS (ESI) 161.0934, $[C_9H_{14}ONa]^+$ requires 161.0937.

*(E)-3-Methyl-1-phenylhept-5-en-1-yn-4-ol (**12b**).* Mesylate **11b** (494 mg) and crotonaldehyde (0.20 mL) with $Pd(PPh_3)_4$ (121 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (20% Et_2O/pentane) yielded **12b** (136 mg, 31%, *dr* > 20:1 by ^1H NMR) as an oil: IR (film) 3417, 2314, 1604 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43−7.41 (m, 2H), 7.30−7.29 (m, 3H), 5.79 (dq, J = 14.7, 7.1 Hz, 1H), 5.57 (ddd, J = 15.3, 7.2, 1.6 Hz, 1H), 3.98 (t, J = 6.7 Hz, 1H), 2.76 (quintet, J = 6.8 Hz, 1H), 2.11 (s, 1H), 1.75 (dd, J = 6.5, 1.1 Hz, 3H), 1.26 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.8, 131.4, 129.3, 128.4, 128.1, 123.4, 90.6, 83.4, 76.1, 34.5, 18.0, 17.3; HRMS (ESI) 223.1089, $[C_{14}H_{16}ONa]^+$ requires 223.1093. NMR data are consistent with the literature.[30]

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J. Org. Chem. 2015, 80, 1042−1051

*(E)-5-tert-Butyloct-2-en-6-yn-4-ol (**12c**) and (E)-5,8,8-trimethylnona-2,5,6-trien-4-ol (**13d**).* Mesylate **11c** (413 mg) and crotonaldehyde (0.30 mL) with $Pd(PPh_3)_4$ (130 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (20% Et_2O/pentane) provided *both* **12c** (63 mg, 17%, *dr* > 20:1 by ^1H NMR) and the allene **13d** (56 mg, 16%, *dr* > 20:1 by ^1H NMR) as oils. For **12c**: IR (film) 3504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.66 (dq, J = 15.3, 6.1 Hz, 1H), 5.59 (ddd, J = 15.3, 6.5, 1.1 Hz, 1H), 4.18 (t, J = 7.7 Hz, 1H), 2.21 (quintet, J = 2.3 Hz, 1H), 1.98 (d, J = 9.4 Hz, 1H), 1.88 (d, J = 2.5 Hz, 3H), 1.70 (d, J = 6.1 Hz, 3H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.5, 126.1, 81.8, 76.1, 70.3, 51.3, 33.9, 28.5, 17.8, 3.7; HRMS (ESI) 203.1402, $[C_{12}H_{20}ONa]^+$ requires 203.1406. For **13d**: IR (film) 3375, 1967 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.72 (dq, J = 15.2, 6.5 Hz, 1H), 5.44 (ddq, J = 15.2, 7.6, 1.5 Hz, 1H), 5.34 (apparent quintet, J = 2.8 Hz, 1H), 4.33−4.30 (m, 1H), 1.79 (d, J = 4.9 Hz, 1H), 1.72 (dd, J = 6.5, 1.5 Hz, 3H), 1.69 (d, J = 2.9 Hz, 3H), 1.04 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 132.3, 128.1, 107.5, 105.2, 73.5, 32.4, 30.3, 17.8, 16.0; HRMS (ESI) 203.1413, $[C_{12}H_{20}ONa]^+$ requires 203.1406.

*(E)-3-tert-Butyl-1-phenylhept-5-en-1-yn-4-ol (**12e**).* Mesylate **11d** (524 mg) and crotonaldehyde (0.20 mL) with $Pd(PPh_3)_4$ (174 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (20% Et_2O/pentane) yielded an inseparable mixture (*dr* 10:1 by ^1H NMR) of diastereomeric alcohols **12e** (157 mg, 33%) as an oil: IR (film) 3467, 2233 cm^{-1}; NMR signals for the major diastereomer, ^1H NMR (500 MHz, $CDCl_3$) δ 7.45−7.43 (m, 2H), 7.31−7.30 (m, 3H), 5.76−5.65 (m, 2H), 4.34−4.31 (m, 1H), 2.48 (d, J = 1.9 Hz, 1H), 1.95 (d, J = 9.6 Hz, 1H), 1.73 (d, J = 5.7 Hz, 3H), 1.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.2, 131.8, 128.4, 128.1, 126.4, 123.5, 87.2, 86.5, 70.6, 51.7, 34.3, 28.6, 17.8; NMR signals discerned for the minor diastereomer, ^1H NMR (500 MHz, $CDCl_3$) δ 5.58−5.52 (m, 1H), 4.75−4.72 (m, 1H), 2.44 (d, J = 2.0 Hz, 1H), 1.15 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.8, 125.4, 65.5, 34.5, 13.5; HRMS (ESI) 265.1569, $[C_{17}H_{22}ONa]^+$ requires 265.1563.

*(E)-5-tert-Butyl-8,8-dimethylnon-2-en-6-yn-4-ol (**12f**).* Mesylate **11e** (503 mg) and crotonaldehyde (0.20 mL) with $Pd(PPh_3)_4$ (130 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (20% Et_2O/pentane) yielded **12f** (137 mg, 30%, *dr* > 20:1 by ^1H NMR) as an oil: IR (film) 3488, 2296 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.65 (dq, J = 15.5, 6.2 Hz, 1H), 5.55 (ddd, J = 15.2, 6.5, 1.4 Hz, 1H), 4.19−4.16 (m, 1H), 2.22 (d, J = 1.8 Hz, 1H), 2.03 (d, J = 10.1 Hz, 1H), 1.70 (d, J = 6.2 Hz, 3H), 1.25 (s, 9H), 1.02 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.5, 125.7, 96.0, 75.2, 69.9, 51.1, 33.8, 31.5, 28.4, 27.8, 17.8; HRMS (ESI) 245.1872, $[C_{15}H_{26}ONa]^+$ requires 245.1876.

*(E)-4,8-Dimethylnon-6-en-2-yn-5-one (**12g**).* Mesylate **11a** (417 mg) and 4-methyl-2-pentenal (0.30 mL) with $Pd(PPh_3)_4$ (130 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (10% Et_2O/pentane) yielded **12g** (130 mg, 33%, *dr* > 20:1 by ^1H NMR) as an oil: IR (film) 3425, 2200 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.68 (ddd, J = 15.5, 6.6, 0.9 Hz, 1H), 5.39 (ddd, J = 15.5, 7.3, 1.3 Hz, 1H), 3.81 (td, J = 6.9, 4.1 Hz, 1H), 2.49−2.43 (m, J = 4.6, 2.3 Hz, 1H), 2.31 (sextet of doublets, J = 6.7, 1.2 Hz, 1H), 2.15 (d, J = 4.2 Hz, 1H), 1.83 (d, J = 2.4 Hz, 3H), 1.11 (d, J = 7.0 Hz, 3H), 1.00 (dd, J = 6.8, 1.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.3, 127.3, 80.1, 78.8, 76.4, 34.0 31.0, 22.4 (2C), 17.7, 3.7; HRMS (ESI) 189.1250, $[C_{11}H_{18}ONa]^+$ requires 189.1250.

*(E)-3,7-Dimethyl-1-phenyloct-5-en-1-yn-4-ol (**12h**).* Mesylate **8b** (458 mg) and 4-methyl-2-pentenal (0.30 mL) with $Pd(PPh_3)_4$ (126 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (10% Et_2O/pentane) yielded an inseparable mixture (*dr* 2:1 by ^1H NMR) of diastereomeric alcohols **12h** (183 mg, 39%) as an oil: IR (film) 3408, 2310 cm^{-1}; NMR signals for the major diastereomer, ^1H NMR (500 MHz, $CDCl_3$) δ 7.42−7.39 (m, 2H), 7.30−7.28 (dd, 3H), 5.74 (dd, J = 15.5, 6.6 Hz, 1H), 5.59 (dd, J = 15.5, 7.1 Hz, 1H), 4.06 (ddd, J = 7.1, 5.1, 4.2 Hz, 1H), 2.92−2.87 (m, 1H), 2.38−2.31 (m, 1H), 1.90 (d, J = 5.2 Hz, 1H), 1.23 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4, 131.8, 128.3, 128.0, 126.4, 123.6, 91.0, 83.1, 75.8, 34.0, 31.1, 22.5(2C), 16.7; NMR signals discernible for the minor diastereomer, ^1H NMR (500 MHz, $CDCl_3$) δ 5.48 (dd, J = 16.4, 7.1 Hz, 1H), 4.00−3.97 (m, 1H), 2.77 (quintet, J = 6.8 Hz, 1H), 2.11 (d, J = 4.5 Hz, 1H), 1.25 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.8, 128.4, 128.1, 127.1, 123.4, 90.7, 83.3, 76.2, 34.5, 31.0, 22.4 (2C), 17.3; HRMS (ESI) 251.1397, $[C_{16}H_{20}ONa]^+$ requires 251.1406.

*(E)-4-tert-Butyl-8-methylnon-6-en-2-yn-5-ol (**12i**) and (E)-2,6,9,9-Tetramethyldeca-3,6,7-trien-5-ol (**13j**).* Mesylate **11c** (412 mg) and 4-methyl-2-pentenal (0.23 mL) with $Pd(PPh_3)_4$ (115 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (10% Et_2O/pentane) provided both **12i** (118 mg, 28%, *dr* > 20:1 by ^1H NMR) and the allene **13j** (126 mg, 30%, *dr* > 20:1 by ^1H NMR) as oils. For **12i**: IR (film) 3429 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.60 (ddd, J = 15.4, 6.5, 0.9 Hz, 1H), 5.49 (ddd, J = 15.4, 6.4, 1.2 Hz, 1H), 4.21−4.17 (m, 1H), 2.29 (sextet, J = 6.7 Hz, 1H), 2.21 (quintet, J = 2.3 Hz, 1H), 1.97 (d, J = 9.3 Hz, 1H), 1.87 (d, J = 2.5 Hz, 3H), 1.03 (s, 9H), 0.99 (dd, J = 6.8, 2.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 130.3, 81.7, 76.2, 70.4, 51.4, 33.9, 30.8, 28.5, 22.4, 3.7; HRMS (ESI) 231.1712, $[C_{14}H_{24}ONa]^+$ 231.1719. For **13j**: IR (film) 3375, 1963 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.68 (dd, J = 15.4, 6.6 Hz, 1H), 5.39−5.33 (m, 2H), 4.33−4.30 (m, 1H), 2.32 (sextet of doublets, J = 6.7, 0.9 Hz, 1H), 1.78 (d, J = 4.9 Hz, 1H), 1.69 (d, J = 2.9 Hz, 3H), 1.04 (s, 9H), 1.00 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 140.2, 128.0, 107.5, 105.2, 73.6, 32.4, 30.9, 30.3, 22.4 (2C), 16.1; HRMS (ESI) 231.1709, $[C_{14}H_{24}ONa]^+$ requires 231.1719.

*(E)-3-tert-Butyl-7-methyl-1-phenyloct-5-en-1-yn-4-ol (**12k**).* Mesylate **11d** (521 mg) and 4-methyl-2-pentenal (0.30 mL) with $Pd(PPh_3)_4$ (121 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (10% Et_2O/pentane) yielded **12k** (148 mg, 28%, *dr* > 20:1 by ^1H NMR) as an oil: IR (film) 3462, 2237 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48−7.46 (m, 2H), 7.35−7.33 (m, 3H), 5.71 (ddd, J = 15.4, 6.4, 1.0 Hz, 1H), 5.61 (ddd, J = 15.4, 6.1, 1.1 Hz, 1H), 4.38 (t, J = 6.6 Hz, 1H), 2.53 (d, J = 2.0 Hz, 1H), 2.36 (sextet, J = 6.7 Hz, 1H), 1.95 (d, J = 9.2 Hz, 1H), 1.17 (s, 9H), 1.05 (dd, J = 6.8, 1.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 131.8, 130.0, 128.4, 128.1, 123.6, 87.4, 86.4, 70.5, 51.8, 34.3, 30.9, 28.7, 22.5; HRMS (ESI) 293.1867, $[C_{19}H_{26}ONa]^+$ requires 293.1876.

*(E)-6-tert-Butyl-2,9,9-trimethyldec-3-en-7-yn-5-ol (**12l**).* Mesylate **11e** (504 mg) and 4-methyl-2-pentenal (0.30 mL) with $Pd(PPh_3)_4$ (119 mg) and $ZnEt_2$ (4.0 mL), and then chromatography (10% Et_2O/pentane) yielded **12l** (157 mg, 31%, *dr* > 20:1 by ^1H NMR) as an oil: IR (film) 3500, 2233 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.60 (ddd, J = 15.4, 6.6, 1.0 Hz, 1H), 5.45 (ddd, J = 15.4, 6.0, 1.2 Hz, 1H), 4.19 (broad s, 1H), 2.30 (sextet, J = 6.7 Hz, 1H), 2.22 (d, J = 1.9 Hz, 1H), 1.98 (br s, 1H), 1.24 (s, 9H), 1.03 (s, 9H), 1.00 (d, J = 6.8 Hz, 3H), 0.99 (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.8, 130.3, 95.8, 75.2, 69.7, 51.2, 33.8, 31.5, 30.8, 28.4, 27.8, 22.5 (2C); HRMS (ESI) 273.2196, $[C_{17}H_{30}ONa]^+$ requires 273.2189.

Preparation of (Alkynylmethyl) Vinyl Ketones and Allenyl Vinyl Ketones (AVKs). Oxidations were based on the procedure of Marshall and Schaaf.[20] (Alkynylmethyl) vinyl alcohol (1 equiv) was added to a solution of Dess−Martin periodinane (DMP) (1.5 equiv) and $NaHCO_3$ (10 equiv) in CH_2Cl_2 (0.1 M with respect to the alcohol). After 1 h equal volumes of saturated aqueous $Na_2S_2O_3$ and saturated $NaHCO_3$ were added and stirred until both the organic and the aqueous layers became clear. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (×2). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by chromatography. (Alkynylmethyl) vinyl ketones were isomerized following the procedure of Harada et al.[31] The (alkynylmethyl) vinyl ketone (1 equiv) was dissolved in CH_2Cl_2 (0.1 M) and treated with NEt_3 (1−10 equiv). After stirring for 1−24 h at rt, the solvent was removed under reduced pressure to provide the AVK. (Because of the instability of the AVKs on silica gel, purification by chromatography was not carried out.)

*(E)-5-Methyloct-2-en-6-yn-4-one and (E)-5-Methylocta-2,5,6-trien-4-one (**14a**).* Enynol **12a** (106 mg) with DMP (493 mg) and $NaHCO_3$ (726 mg), then chromatography (10% Et_2O/pentane) gave the (alkynylmethyl) vinyl ketone (46 mg, 44%) as an oil: IR (film) 2238, 1708, 1638 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.01 (dq, J = 15.5, 6.9 Hz, 1H), 6.46 (dq, J = 15.5, 1.6 Hz, 1H), 3.41 (qq, J = 7.1, 2.4

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J. Org. Chem. 2015, 80, 1042−1051

Hz, 1H), 1.93 (dd, J = 6.9, 1.7 Hz, 3H), 1.83 (d, J = 2.5 Hz, 3H), 1.32 (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.6, 144.0, 128.5, 79.8, 77.6, 37.7, 18.5, 17.2, 3.9; HRMS (ESI) 159.0781, $[C_9H_{12}ONa]^+$ requires 159.0780. The (alkynylmethyl) vinyl ketone (84 mg) with NEt_3 (85 μL) for 2 h provided AVK **14a** (15 mg, 18%) as an oil: IR (film) 1950, 1667, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (dq, J = 14.9, 7.3 Hz, 1H), 6.72 (dd, J = 15.3, 1.5 Hz, 1H), 5.54−5.49 (m, J = 2.3 Hz, 1H), 1.88 (dd, J = 6.8, 1.4 Hz, 3H), 1.83−1.81 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.7, 190.5, 141.3, 127.0, 104.4, 89.3, 18.2, 13.9, 13.6; HRMS (ESI) 159.0773, $[C_9H_{12}ONa]^+$ requires 159.0780.

*(E)-3-Methyl-1-phenylhept-5-en-1-yn-4-one and (E)-3-Methyl-1-phenylhepta-1,2,5-trien-4-one (**14b**).* Enynol **12b** (104 mg) with DMP (304 mg) and $NaHCO_3$ (488 mg), then chromatography (20% Et_2O/pentane) gave 36 mg (35%) of an oil that was an inseparable mixture of the (alkynylmethyl) vinyl ketone and **14b** in a 1.5:1 ratio (respectively) by ^{1}H NMR. NMR data for the (alkynylmethyl) vinyl ketone: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43−7.40 (m, 2H), 7.39−7.34 (m, 1H), 7.32−7.28 (m, 2H), 7.07 (dq, J = 15.5, 6.9 Hz, 1H), 6.57−6.53 (m, 1H), 3.67 (q, J = 7.0 Hz, 1H), 1.94 (dd, J = 6.9, 1.7 Hz, 3H), 1.43 (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.7, 144.5, 131.8, 129.1, 128.4, 128.4, 128.3, 88.1, 84.1, 38.3, 18.6, 16.9. The 1.5:1 mixture of the (alkynylmethyl) vinyl ketone and **14b** (25 mg) with NEt_3 (0.10 mL) for 1 h afforded homogeneous AVK **14b** (25 mg, 99%) as an oil: IR (film) 1938, 1717, 1671, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.36 (m, 2H), 7.33−7.29 (m, 3H), 6.96 (dq, J = 15.2, 6.9 Hz, 1H), 6.72 (dq, J = 15.2, 1.6 Hz, 1H), 6.57 (q, J = 2.7 Hz, 1H), 1.98 (d, J = 2.8 Hz, 3H), 1.84 (dd, J = 6.9, 1.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.7, 189.6, 142.8, 132.8, 129.5, 128.3, 127.7, 127.4, 108.8, 98.4, 18.6, 14.1; HRMS (ESI) 221.0931, $[C_{14}H_{14}ONa]^+$ requires 221.0937.

*(E)-5-tert-Butyloct-2-en-6-yn-4-one and (E)-5-tert-Butylocta-2,5,6-trien-4-one (**14c**).* Enynol **12c** (103 mg) with DMP (414 mg) and $NaHCO_3$ (633 mg), then chromatography (10% Et_2O/pentane) provided the (alkynylmethyl) vinyl ketone (73 mg, 72%) as an oil: IR (film) 2238, 1692, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.91 (dq, J = 15.0, 7.3 Hz, 1H), 6.49 (dq, J = 15.4, 1.6 Hz, 1H), 3.17 (q, J = 2.4 Hz, 1H), 1.91 (dd, J = 6.9, 1.5 Hz, 3H), 1.87 (d, J = 2.5 Hz, 3H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 143.0, 130.2, 81.5, 75.9, 55.1, 35.0, 28.1, 18.4, 3.9; HRMS (ESI) 201.1242, $[C_{12}H_{18}ONa]^+$ requires 201.1250. The (alkynylmethyl) vinyl ketone (65 mg) with NEt_3 (0.5 mL) for 12 h gave AVK **14c** (15 mg, 18%) as an oil: IR (film) 1941, 1675, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (dq, J = 15.2, 6.9 Hz, 1H), 6.65 (d, J = 15.3 Hz, 1H), 5.52 (q, J = 7.2 Hz, 1H), 1.86 (d, J = 7.0 Hz, 3H), 1.81 (d, J = 7.2 Hz, 3H), 1.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.0, 190.4, 140.9, 129.5, 117.8, 90.7, 33.7, 29.7, 18.3, 13.9; HRMS 201.1241, $[C_{12}H_{18}ONa]^+$ requires 201.1250.

*(E)-5,8,8-Trimethylnona-2,5,6-trien-4-one (**14d**).* Trienol **13d** (141 mg) with DMP (489 mg) and $NaHCO_3$ (648 mg), then chromatography (5% Et_2O/pentane) yielded AVK **14d** (58 mg, 42%) as an oil: IR (film) 1950, 1675, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89 (dq, J = 15.2, 6.8 Hz, 1H), 6.76 (dq, J = 15.3, 1.5 Hz, 1H), 5.54 (q, J = 2.7 Hz, 1H), 1.87 (dd, J = 6.8, 1.5 Hz, 3H), 1.85 (d, J = 2.7 Hz, 3H), 1.13 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.1, 194.7, 141.3, 126.9, 106.9, 106.1, 33.5, 30.3, 18.3, 14.1; HRMS (ESI) 201.1241, $[C_{12}H_{18}ONa]^+$ requires 201.1250.

*(E)-3-tert-Butyl-1-phenylhept-5-en-1-yn-4-one and (E)-3-tert-Butyl-1-phenylhepta-1,2,5-trien-4-one (**14e**).* Enynol **12e** (134 mg) with DMP (395 mg) and $NaHCO_3$ (503 mg), then chromatography (10% Et_2O/pentane) yielded the (alkynylmethyl) vinyl ketone (90 mg, 69%) as an oil: IR (film) 2317, 1692, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.43 (m, 2H), 7.31−7.30 (m, 3H), 6.97 (dq, J = 15.4, 6.9 Hz, 1H), 6.59 (dd, J = 15.4, 1.6 Hz, 1H), 3.40 (s, 1H), 1.91 (dd, J = 6.9, 1.6 Hz, 3H), 1.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.9, 143.5, 131.8, 129.9, 128.4, 128.2, 123.5, 86.7, 86.3, 55.9, 35.5, 28.3, 18.5; HRMS (ESI) 263.1409, $[C_{17}H_{20}ONa]^+$ requires 263.1406. The (alkynylmethyl) vinyl ketone (78 mg) with NEt_3 (50 μL) for 4 h provided AVK **14e** (77 mg, 99%) as an oil: IR (film) 1925, 1714, 1671, 1625 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, J = 7.5 Hz, 2H), 7.31−7.28 (m, 2H), 7.26−7.25 (m, 1H), 6.87 (dq, J = 15.2, 6.8 Hz, 1H), 6.62 (dd, J = 15.2, 1.5 Hz, 1H), 6.57 (s, 1H), 1.80 (dd, J = 6.9, 1.4 Hz, 3H), 1.27 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.3, 189.1, 142.1, 133.0, 129.5 129.2, 127.9, 127.1, 121.8, 99.4, 34.9, 29.8, 18.3; HRMS (ESI) 263.1397, $[C_{17}H_{20}ONa]^+$ requires 263.1406.

*(E)-5-tert-Butyl-8,8-dimethylnon-2-en-6-yn-4-one and (E)-5-tert-Butyl-8,8-dimethylnona-2,6,7-trien-4-one (**14f**).* Enynol **12f** (114 mg) with DMP (328 mg) and $NaHCO_3$ (420 mg), then chromatography (10% Et_2O/pentane) afforded the (alkynylmethyl) vinyl ketone (42 mg, 37%) as an oil: IR (film) 2242, 1692, 1625 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.90 (dq, J = 15.4, 6.9 Hz, 1H), 6.55 (dq, J = 15.4, 1.6 Hz, 1H), 3.09 (s, 1H), 1.90 (dd, J = 6.9, 1.7 Hz, 3H), 1.24 (s, 9H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9, 142.5, 129.8, 95.2, 75.5, 55.4, 34.9, 31.2, 28.1, 27.8, 18.4; HRMS (ESI) 243.1719, $[C_{15}H_{24}ONa]^+$ requires 243.1719. The (alkynylmethyl) vinyl ketone (34 mg) with NEt_3 (0.5 mL) for 15 h yielded AVK **14f** (20 mg, 59%) as an oil: IR (film) 1942, 1675, 1633 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.81 (dq, J = 15.2, 6.5 Hz, 1H), 6.73 (dq, J = 15.2, 1.3 Hz, 1H), 5.55 (s, 1H), 1.85 (dd, J = 6.5, 1.3 Hz, 3H), 1.19 (s, 9H), 1.13 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.2, 189.8, 140.5, 129.0, 120.0, 107.1, 33.4, 33.2, 30.1, 29.7, 18.2; HRMS (ESI) 243.1708, $[C_{15}H_{24}ONa]^+$ requires 243.1719.

*(E)-4,8-Dimethylnon-6-en-2-yn-5-one and (E)-4,8-Dimethylnona-2,3,6-trien-5-one (**14g**).* Enynol **12g** (105 mg) with DMP (414 mg) and $NaHCO_3$ (501 mg), then chromatography (20% Et_2O/pentane) yielded the (alkynylmethyl) vinyl ketone (94 mg, 91%) as an oil: IR (film) 2350, 1704, 1633 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (dd, J = 15.7, 6.7 Hz, 1H), 6.37 (d, J = 15.7 Hz, 1H), 3.45−3.41 (m, 1H), 2.49 (octet, J = 6.8 Hz, 1H), 1.83 (d, J = 1.7 Hz, 3H), 1.32 (d, J = 7.1 Hz, 3H), 1.09 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 154.9, 124.1, 79.7, 77.7, 37.7, 31.4, 21.4, 17.2, 3.8; HRMS (ESI) 187.1090, $[C_{11}H_{16}ONa]^+$ requires 187.1093. The (alkynylmethyl) vinyl ketone (81 mg) with NEt_3 (69 μL) for 24 h gave AVK **14g** (44 mg, 54%) as an oil: IR (film) 1950, 1671, 1625 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.84 (dd, J = 15.5, 6.9 Hz, 1H), 6.65 (d, J = 15.5 Hz, 1H), 5.54−5.48 (m, 1H), 2.45 (octet, J = 6.8 Hz, 1H), 1.83−1.81 (m, 6H), 1.06 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.7, 191.0, 152.4, 122.7, 104.6, 89.3, 31.2, 21.6, 14.0, 13.6; HRMS (ESI) 187.1085, $[C_{11}H_{16}ONa]^+$ requires 187.1093.

*(E)-3,7-Dimethyl-1-phenyloct-5-en-1-yn-4-one and (E)-3,7-Dimethyl-1-phenylocta-1,2,5-trien-4-one (**14h**).* Enynol **12h** (116 mg) with DMP (298 mg) and $NaHCO_3$ (420 mg), then chromatography (10% Et_2O/pentane) provided the (alkynylmethyl) vinyl ketone (87 mg, 76%) as an oil: IR (film) 2312, 1700, 1638 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.40 (m, 2H), 7.31−7.29 (m, 3H), 7.03 (dd, J = 15.7, 6.7 Hz, 1H), 6.47 (dd, J = 15.7, 1.3 Hz, 1H), 3.69 (q, J = 7.0 Hz, 1H), 2.51 (octet of doublets, J = 6.8, 1.3 Hz, 1H), 1.45 (d, J = 7.0 Hz, 3H), 1.10 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.3, 155.4, 131.7, 128.4, 128.2, 124.1, 123.3, 88.2, 84.1, 38.3, 31.4, 21.4, 16.9; HRMS (ESI) 249.1246, $[C_{16}H_{18}ONa]^+$ requires 249.1250. The (alkynylmethyl) vinyl ketone (74 mg) with NEt_3 (0.5 mL) for 1 h gave AVK **14h** (74 mg, 99%) as an oil: IR (film) 1938, 1708, 1675, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (t, J = 7.5 Hz, 2H), 7.31−7.26 (m, 3H), 6.88 (dd, J = 15.4, 7.1 Hz, 1H), 6.63 (d, J = 15.4 Hz, 1H), 6.56 (q, J = 2.7 Hz, 1H), 2.40 (octet, J = 6.8 Hz, 1H), 1.97 (d, J = 2.7 Hz, 3H), 1.00 (d, J = 6.7 Hz, 3H), 0.99 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.4, 189.9, 153.5, 132.5, 129.1, 127.9, 127.3, 122.9, 108.5, 98.0, 31.3, 21.6 (2C), 13.9; HRMS (ESI) 249.1246, $[C_{16}H_{18}ONa]^+$ requires 249.1250.

*(E)-4-tert-Butyl-8-methylnon-6-en-2-yn-5-one and (E)-4-tert-Butyl-8-methylnona-2,3,6-trien-5-one (**14i**).* Enynol **12i** (64 mg) with DMP (168 mg) and $NaHCO_3$ (255 mg), then chromatography (10% Et_2O/pentane) provided the (alkynylmethyl) vinyl ketone (48 mg, 76%) as an oil: IR (film) 2317, 1692, 1629 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (dd, J = 15.6, 6.8 Hz, 1H), 6.39 (dd, J = 15.6, 1.4 Hz, 1H), 3.20 (q, J = 2.5 Hz, 1H), 2.47 (octet of doublets, J = 6.8, 1.4 Hz, 1H), 1.86 (d, J = 2.5 Hz, 3H), 1.07 (d, J = 6.8 Hz, 3H), 1.07 (d, J = 6.8 Hz, 3H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 153.8, 126.1, 81.4, 75.9, 55.1, 35.0, 31.3, 28.1, 21.5 (2C), 3.9; HRMS (ESI) 229.1553, $[C_{14}H_{22}ONa]^+$ requires 229.1563. The (alkynylmeth-

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J. Org. Chem. 2015, 80, 1042−1051

yl) vinyl ketone (71 mg) with NEt_3 (0.3 mL) for 2 h yielded AVK **14i** (71 mg, 99%) as an oil: IR (film) 1946, 1675, 1625 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.76 (dd, J = 15.5, 6.8 Hz, 1H), 6.58 (dd, J = 15.5, 1.3 Hz, 1H), 5.52 (q, J = 7.2 Hz, 1H), 2.43 (octet of doublets, J = 6.8, 1.3 Hz, 1H), 1.81 (d, J = 7.2 Hz, 3H), 1.18 (s, 9H), 1.05 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 211.9, 190.8, 152.0, 125.1, 117.8, 90.5, 33.6, 31.1, 29.6, 21.6 (2C), 13.8; HRMS (ESI) 229.1555, $[C_{14}H_{22}ONa]^+$ requires 229.1563.

*(E)-2,6,9,9-Tetramethyldeca-3,6,7-trien-5-one (**14j**).* Trienol **12j** (121 mg) with DMP (365 mg) and $NaHCO_3$ (531 mg), then chromatography (5% Et_2O/pentane) yielded AVK **14j** (61 mg, 51%) as an oil: IR (film) 1950, 1675, 1629 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.85 (dd, J = 15.5, 6.3 Hz, 1H), 6.70 (dd, J = 15.5, 1.4 Hz, 1H), 5.52 (q, J = 2.7 Hz, 1H), 2.43 (octet of doublets, J = 6.7, 1.3 Hz, 1H), 1.84 (d, J = 2.7 Hz, 3H), 1.12 (s, 9H), 1.05 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.1, 190.7, 152.1, 122.5, 106.1, 102.8, 33.4, 31.1, 30.2, 21.5, 21.4, 14.0; HRMS (ESI) 229.1558, $[C_{14}H_{22}ONa]^+$ requires 229.1563.

*(E)-3-tert-Butyl-7-methyl-1-phenyloct-5-en-1-yn-4-one and (E)-3-tert-Butyl-7-methyl-1-phenylocta-1,2,5-trien-4-one (**14k**).* Enynol **12k** (138 mg) with DMP (351 mg) and $NaHCO_3$ (591 mg), then chromatography (10% Et_2O/pentane) yielded the (alkynylmethyl) vinyl ketone (119 mg, 87%) as an oil: IR (film) 2213, 1638 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44−7.42 (m, 2H), 7.31−7.30 (m, 3H), 6.92 (dd, J = 15.6, 6.7 Hz, 1H), 6.52 (dd, J = 15.6, 1.3 Hz, 1H), 3.43 (s, 1H), 2.49 (octet of doublets, J = 6.8, 1.3 Hz, 1H), 1.12 (s, 9H), 1.08 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 154.3, 131.7, 128.4, 128.2, 125.7, 123.6, 86.8, 86.2, 56.0, 35.5, 31.3, 28.3, 21.5 (2C); HRMS (ESI) 291.1727, $[C_{19}H_{24}ONa]^+$ requires 291.1719. The (alkynylmethyl) vinyl ketone (121 mg) with NEt_3 (69 μL) for 15 h afforded AVK **14k** (98 mg, 81%) as an oil: IR (film) 1925, 1713, 1675, 1625 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 (t, J = 7.5 Hz, 2H), 7.31−7.29 (m, 2H), 7.27−7.24 (m, 1H), 6.79 (dd, J = 15.4, 7.1 Hz, 1H), 6.57 (s, 1H), 6.52 (dd, J = 15.4, 1.2 Hz, 1H), 2.36 (octet of doublets, J = 6.8, 1.1 Hz, 1H), 1.27 (s, 9H), 0.96 (d, J = 6.4 Hz, 3H), 0.95 (d, J = 6.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.2, 189.8, 153.1, 133.0, 129.1, 127.8, 127.0, 125.3, 121.8, 99.3, 34.8, 31.2, 29.7, 21.6 (2C); HRMS (ESI) 291.1711, $[C_{19}H_{24}ONa]^+$ requires 291.1719.

*(E)-6-tert-Butyl-2,9,9-trimethyldec-3-en-7-yn-5-one and (E)-6-tert-Butyl-2,9,9-trimethyl-deca-3,6,7-trien-5-one (**14l**).* Enynol **12l** (143 mg) with DMP (460 mg) and $NaHCO_3$ (638 mg), then chromatography (10% Et_2O/pentane) gave the (alkynylmethyl) vinyl ketone (118 mg, 83%) as an oil: IR (film) 2242, 1692, 1629 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.87 (dd, J = 15.6, 6.4 Hz, 1H), 6.52 (dd, J = 15.6, 1.3 Hz, 1H), 3.09 (s, 1H), 2.47 (octet of doublets, J = 6.7, 1.2 Hz, 1H), 1.24 (s, 9H), 1.07 (d, J = 6.8 Hz, 6H), 1.03 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 153.3, 125.4, 95.2, 75.7, 55.7, 34.9, 31.2 (2C), 28.1, 27.8, 21.4; HRMS (ESI) 271.2041, $[C_{17}H_{28}ONa]^+$ requires 271.2032. The (alkynylmethyl) vinyl ketone (104 mg) with NEt_3 (0.5 mL) for 12 h provided AVK **14l** (64 mg, 61%) as an oil: IR (film) 1942, 1671, 1625 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.79 (dd, J = 15.5, 6.1 Hz, 1H), 6.69 (dd, J = 15.5, 1.3 Hz, 1H), 5.55 (s, 1H), 2.43 (octet of doublets, J = 6.6, 1.3 Hz, 1H), 1.20 (s, 9H), 1.13 (s, 9H), 1.04 (d, J = 6.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3, 190.2, 151.5, 124.6, 120.3, 107.1, 33.4, 33.2, 31.0, 30.1, 29.7, 21.5 (2C); HRMS (ESI) 271.2028, $[C_{17}H_{28}ONa]^+$ requires 271.2032.

Nazarov Reactions with (4 + 3)-Cyclizations. The allenyl vinyl ketone (1 equiv) and 2,3-dimethyl-1,3-butadiene (5 equiv) were dissolved in CH_2Cl_2 (sufficient to make a 0.1 M solution of the AVK) and cooled to −78 °C. $BF_3{\cdot}OEt_2$ (1 equiv) was added as a 1 M solution in CH_2Cl_2. After 5−10 min the reaction was quenched by the addition of a saturated solution of $NaHCO_3$, and the mixture was allowed to warm to rt. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (×2). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by chromatography.

(1R,6R*,7S*,8Z)-8-Ethylidene-1,3,4,7-tetramethylbicyclo[4.2.1]-bicyclonon-3-en-9-one (**15a**) and (1R*,6R*,7S*,8E)-8-Ethylidene-1,3,4,7-tetramethylbicyclo[4.2.1]bicyclonon-3-en-9-one (**16a**).* AVK **14a** (46 mg) and the diene (0.20 mL) with $BF_3{\cdot}OEt_2$ (0.35 mL), then chromatography (3% Et_2O/pentane) yielded **15a** and **16a** (49 mg, 66%), an oil, as an inseparable mixture of isomers in a 74:26 ratio (by ^1H NMR), respectively. Data for the mixture: IR (film) 1750 cm^{-1}; HRMS (ESI) 241.1564, $[C_{15}H_{22}ONa]^+$ requires 241.1563. For **15a**: ^1H NMR (500 MHz, $CDCl_3$) δ 5.37 (q, J = 7.2 Hz, 1H), 2.36−2.21 (m, 5H), 2.14 (br d, J = 16.4 Hz, 1H), 1.73 (d, J = 7.2 Hz, 3H), 1.71 (s, 3H), 1.66 (s, 3H), 1.37 (s, 3H), 0.95 (d, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.4, 148.7, 127.7, 125.6, 118.5, 55.1, 51.3, 47.5, 41.3, 39.6, 24.4, 24.1, 23.7, 21.5, 14.0. NMR signals that could be discerned for the minor isomer **16a**: ^1H NMR (500 MHz, $CDCl_3$) δ 5.27 (qd, J = 6.9, 1.7 Hz, 1H), 2.61 (q, J = 7.2 Hz, 1H), 1.90 (d, J = 15.6 Hz, 1H), 1.60−1.59 (m, 6H), 1.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 127.7, 115.3, 55.7, 52.2, 51.9, 39.5, 37.5, 24.0, 23.8, 22.1, 21.2, 13.7.

(1R,6R*,7S*,8Z)-1,3,4,7-Tetramethyl-8-(phenylmethylene)-bicyclo[4.2.1]non-3-en-9-one (**15b**).* AVK **14b** (13 mg) and the diene (37 μL) with $BF_3{\cdot}OEt_2$ (66 μL), then chromatography (3% Et_2O/pentane) gave **15b** (12 mg, 65%) as an oil: IR (film) 1750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, J = 7.8 Hz, 2H), 7.23 (t, J = 7.4 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 6.55 (s, 1H), 2.53 (q, J = 7.2 Hz, 1H), 2.40 (br d, J = 15.5 Hz, 1H), 2.35−2.29 (m, 2H), 2.18 (d, J = 15.8 Hz, 1H), 2.12 (br d, J = 15.8 Hz, 1H), 1.76 (s, 6H), 1.13 (d, J = 7.3 Hz, 3H), 0.96 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 223.6, 151.3, 137.9, 128.9, 127.9, 127.2, 126.6, 126.5, 125.1, 54.4, 53.2, 50.0, 41.2, 39.7, 24.3, 24.0, 23.7, 21.0; HRMS (ESI) 303.1711, $[C_{20}H_{24}ONa]^+$ requires 303.1719.

(1R,6R*,7S*,8Z)-1-tert-Butyl-8-ethylidene-3,4,7-trimethyl-bicyclo[4.2.1]non-3-en-9-one (**15c**).* AVK **14c** (48 mg) and the diene (0.15 mL) with $BF_3{\cdot}OEt_2$ (0.30 mL), then chromatography (3% Et_2O/pentane) provided **15c** (33 mg, 47%) as an oil: IR (film) 1742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.63 (q, J = 7.5 Hz, 1H), 2.65 (br d, J = 15.7 Hz, 1H), 2.40−2.35 (m, 3H), 2.20−2.16 (m, 2H), 1.72−1.70 (m, 9H), 1.16 (s, 9H), 1.07 (d, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 226.9, 146.5, 126.6, 124.9, 123.7, 61.2, 56.1, 46.4, 41.9, 41.5, 37.5, 28.9, 24.1, 23.9, 22.7, 18.1; HRMS (ESI) 283.2034, $[C_{18}H_{28}ONa]^+$ requires 283.2032. Exposure of a 0.1 M solution of **15c** (20 mg) in CH_2Cl_2 to $BF_3{\cdot}OEt_2$ (0.1 mL) for 30 min at rt returned only **15c** (16 mg) after workup as described in the Nazarov procedure.

(1R,6R*,7S*,8Z)-8-(2,2-Dimethylpropylidene)-1,3,4,7-tetramethylbicyclo[4.2.1]non-3-en-9-one (**15d**).* AVK **14d** (43 mg) and the diene (0.15 mL) with $BF_3{\cdot}OEt_2$ (0.24 mL), then chromatography (3% Et_2O/pentane) yielded **15d** (31 mg, 49%) as an oil: IR (film) 1746 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.34 (s, 1H), 2.40 (d, J = 16.0 Hz, 1H), 2.36 (br d, $J \approx$ 15 Hz, 1H), 2.27−2.20 (m, 3H), 2.10 (br d, J = 16.0 Hz, 1H), 1.70 (s, 3H), 1.67 (s, 3H), 1.39 (s, 3H), 1.14 (s, 9H), 0.95 (d, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.3, 144.5, 136.9, 126.8, 126.2, 54.0, 51.6, 48.9, 43.5, 39.7, 33.0, 32.4, 25.3, 23.9, 23.8, 23.0; HRMS (ESI) 283.2024, $[C_{18}H_{28}ONa]^+$ requires 283.2032.

(1R,6R*,7S*,8Z)-1-tert-Butyl-8-(phenylmethylene)-3,4,7-trimethylbicyclo[4.2.1]non-3-en-9-one (**15e**) and (1R*,6R*,7S*,8E)-1-tert-Butyl-8-(phenylmethylene)-3,4,7-trimethylbicyclo[4.2.1]non-3-en-9-one (**16e**).* AVK **14e** (77 mg) and the diene (0.20 mL) with $BF_3{\cdot}OEt_2$ (0.35 mL), then chromatography (3% Et_2O/pentane) provided **15e** (59 mg, 56%) as an oil: IR (film) 1742 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 7.4 Hz, 1H), 7.09 (d, J = 7.9 Hz, 2H), 6.72 (s, 1H), 2.64 (br d, J = 16.3 Hz, 1H), 2.60−2.50 (m, 3H), 2.29 (dd, J = 5.1, 3.6 Hz, 1H), 2.26 (br d, J = 17.1 Hz, 1H), 1.84 (s, 3H), 1.72 (s, 3H), 1.22 (d, J = 7.5 Hz, 3H), 0.85 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 225.4, 149.5, 140.5, 128.6, 128.1, 127.9, 126.3 (2C), 124.9, 62.0, 55.4, 46.9, 45.7, 41.9, 37.5, 28.8, 23.8, 23.7, 23.5; HRMS (ESI) 345.2186, $[C_{23}H_{30}ONa]^+$ requires 345.2189. Exposure of a 0.1 M solution of **15e** (25 mg) in CH_2Cl_2 to $BF_3{\cdot}OEt_2$ (0.1 mL) for 30 min at rt returned an inseparable mixture of **15e** and **16e** (20:80 by ^1H NMR, 20 mg) after workup as described in the Nazarov procedure. For **16e** (from the spectra of the mixture): ^1H NMR (500 MHz, $CDCl_3$) δ 7.33 (t, J = 7.7 Hz, 2H), 7.27−7.24 (m, 1H), 7.21 (d, J = 7.9 Hz, 3H), 6.45 (s, 1H), 2.74 (q, J = 7.3 Hz, 1H), 2.45−2.33 (m, 3H), 2.19−2.18 (m,

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J. Org. Chem. 2015, 80, 1042−1051

2H), 1.69 (s, 3H), 1.67 (s, 3H), 1.20 (s, 9H), 1.05 (d, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 225.0, 151.2, 138.3, 128.63, 128.45, 126.4, 125.78, 125.76, 60.7, 56.9, 44.4, 40.2, 38.5, 36.0, 27.6, 24.2, 24.0, 21.1.

(1R,6R*,7S*,8Z)-8-Ethylidene-7-isopropyl-1,3,4-trimethylbicyclo[4.2.1]non-3-en-9-one (**15g**).* AVK **14g** (34 mg) and the diene (0.12 mL) with BF_3·OEt_2 (0.21 mL), then chromatography (3% Et_2O/pentane) gave **15g** (36 mg, 71%) as an oil: IR (film) 1750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40 (qd, J = 7.2, 1.3 Hz, 1H), 2.40−2.37 (m, 2H), 2.35 (d, J = 16.0 Hz, 1H), 2.16 (dd, J = 16.5, 6.5 Hz, 1H), 2.14−2.10 (m, 2H), 1.76 (dd, J = 7.2, 1.2 Hz, 3H), 1.72 (s, 3H), 1.72 (overlapped, 1H), 1.67 (s, 3H), 1.37 (s, 3H), 0.85 (d, J = 6.9 Hz, 3H), 0.65 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 225.0, 146.3, 127.8, 125.7, 119.3, 52.9, 52.3, 48.9, 47.7, 40.5, 34.4, 24.2, 23.7, 20.7, 20.4, 17.8, 13.9; HRMS (ESI) 269.1872, $[C_{17}H_{26}ONa]^+$ requires 269.1876.

(1R,6R*,7S*,8Z)-7-Isopropyl-1,3,4-trimethyl-8-(phenylmethylene)bicyclo[4.2.1]non-3-en-9-one (**15h**).* AVK **14h** (74 mg) and the diene (0.20 mL) with BF_3·OEt_2 (0.35 mL), then chromatography (3% Et_2O/pentane) yielded **15h** (49 mg, 49%) as an oil: IR (film) 1756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, J = 7.5 Hz, 2H), 7.24 (t, J = 7.3 Hz, 1H), 7.19 (d, J = 7.5 Hz, 2H), 6.61 (s, 1H), 2.48−2.45 (m, 2H), 2.35 (narrow m, 1H), 2.23 (dd, J = 17.0, 6.9 Hz, 1H), 2.18 (d, J = 16.1 Hz, 1H), 2.10 (br d, J = 16.0 Hz, 1H), 1.99 (m, 1H), 1.78 (s, 6H), 0.97 (d, J = 6.8 Hz, 3H), 0.93 (s, 3H), 0.72 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.2, 149.1, 138.1, 128.9, 127.9, 127.2, 126.6 (2C), 125.4, 54.2, 52.2, 50.2, 47.7, 40.7, 34.4, 24.2, 23.8, 21.0, 20.1, 17.2; HRMS (ESI) 331.2030, $[C_{22}H_{28}ONa]^+$ requires 331.2032.

(1R,6R*,7S*,8Z)-1-tert-Butyl-8-ethylidene-7-isopropyl-3,4-dimethylbicyclo[4.2.1]non-3-en-9-one (**15i**).* AVK **14i** (23 mg) and the diene (54 μL) with BF_3·OEt_2 (0.10 mL), then chromatography (3% Et_2O/pentane) gave **15i** (19 mg, 59%) as an oil: IR (film) 1742 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.55 (q, J = 7.2 Hz, 1H), 2.66 (d, J = 16.2 Hz, 1H), 2.45−2.42 (m, 2H), 2.36 (br d, J = 16.1 Hz, 1H), 2.10 (br dd, J = 17.9, 5.0 Hz, 1H), 1.71−1.66 (m, 10H), 1.39−1.31 (m, 1H), 1.10 (s, 9H), 0.92 (d, J = 6.6 Hz, 3H), 0.88 (d, J = 6.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 226.6, 142.8, 127.5, 126.0, 125.1, 61.0, 60.4, 53.5, 42.2, 41.9, 37.8, 30.1, 28.6, 23.8, 23.6, 21.8, 21.0, 17.9; HRMS (ESI) 311.2357, $[C_{20}H_{32}ONa]^+$ requires 311.2345.

(1R,6R*,7S*,8Z)-8-(2,2-Dimethylpropylidene)-7-isopropyl-1,3,4-trimethylbicyclo[4.2.1]-non-3-en-9-one (**15j**).* AVK **14j** (61 mg) and the diene (0.20 mL) with BF_3·OEt_2 (0.30 mL), then chromatography (3% Et_2O/pentane) gave **15j** (31 mg, 36%) as an oil: IR (film) 1750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40 (d, J = 1.5 Hz, 1H), 2.42−2.36 (m, 3H), 2.14 (dd, J = 15.9, 5.8 Hz, 1H), 2.07 (br d, J = 16.0 Hz, 1H), 2.03 (narrow m, 1H), 1.79−1.73 (m, 1H), 1.71 (s, 3H), 1.68 (s, 3H), 1.40 (s, 3H), 1.16 (s, 9H), 0.88 (d, J = 6.9 Hz, 3H), 0.58 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.9, 142.6, 137.0, 127.2, 126.4, 54.0, 52.9, 49.3, 47.2, 40.8, 35.1, 33.1, 32.5, 24.1, 24.0, 21.7, 21.1, 16.9; HRMS (ESI) 311.2358, $[C_{20}H_{32}ONa]^+$ requires 311.2345.

(1R,6R*,7S*,8Z)-1-tert-Butyl-7-isopropyl-3,4-dimethyl-8-(phenylmethylene)bicyclo[4.2.1]-non-3-en-9-one (**15k**).* AVK **14k** (25 mg) and the diene (53 μL) with BF_3·OEt_2 (0.10 mL), then chromatography (3% Et_2O/pentane) yielded **15k** (25 mg, 77%) as an oil: IR (film) 1738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 (t, J = 7.5 Hz, 2H), 7.17 (t, J = 7.4 Hz, 1H), 7.09 (d, J = 7.5 Hz, 2H), 6.67 (s, 1H), 2.61−2.58 (m, 2H), 2.49 (br d, J = 16.8 Hz, 1H), 2.22 (br d, J = 13.2 Hz, 1H), 2.03−1.97 (m, 2H), 1.80 (s, 3H), 1.71 (s, 3H), 1.52−1.47 (m, 1H), 1.13 (d, J = 6.6 Hz, 3H), 0.98 (d, J = 6.3 Hz, 3H), 0.85 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 224.8, 145.5, 140.4, 131.5, 128.7, 127.7, 126.5, 126.3, 124.5, 61.8, 61.1, 53.2, 45.8, 42.3, 37.7, 30.5, 28.8, 23.4 (2C), 22.0, 21.2; HRMS (ESI) 373.2497, $[C_{25}H_{34}ONa]^+$ requires 373.2502.

(1R,2Z,3S*,6R*)-2-Ethylidene-6-(3,4-dimethoxyphenyl)-1,3-dimethylbicyclo[2.2.1]heptan-7-one (**17**) and (1R*,2E,3S*,6R*)-2-Ethylidene-6-(3,4-dimethoxyphenyl)-1,3-dimethylbicyclo[2.2.1]-heptan-7-one (**18**).* AVK **14a** (30 mg, 0.22 mmol) and 3,4-dimethoxystyrene (0.10 mL, 0.68 mmol) were dissolved in CH_2Cl_2 (2.0 mL). The solution was cooled to −78 °C, and BF_3·OEt_2 (0.25 mL, 0.22 mmol) was added. After 15 min the reaction was quenched by the addition of a saturated solution of $NaHCO_3$. After warming to rt the phases were separated, and the aqueous phase was extracted with CH_2Cl_2 (×2). The combined organic extracts were dried over Na_2SO_4, filtered and concentrated under reduced pressure. Chromatography (40% Et_2O/pentane) of the residue gave 43 mg (65%) of an oil that was an inseparable mixture (79:21 by ^{1}H NMR) of diastereomers **17** and **18**. Data for the mixture: IR (film) 1751 cm^{-1}; HRMS (ESI) 323.1631, $[C_{19}H_{24}O_3Na]^+$ requires 323.1618. For **17**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.77 (d, J = 8.2 Hz, 1H), 6.59−6.55 (m, 1H), 6.50 (d, J = 2.0 Hz, 1H), 5.39−5.34 (m, 1H), 3.85 (s, 6H), 3.02 (dd, J = 10.5, 3.9 Hz, 1H), 2.56 (q, J = 7.1 Hz, 1H), 2.23−2.17 (m, 1H), 2.13−2.09 (m, 2H), 1.75 (dd, J = 7.2 Hz, 1.3 Hz, 3H), 1.04 (d, J = 7.1 Hz, 3H), 0.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.2, 149.0, 145.3, 135.8, 120.3, 118.5, 114.9, 111.2, 111.1, 56.0 (2C), 52.4, 47.8, 47.5, 42.6, 33.4, 21.3, 13.7, 12.4. Discernable NMR signals for **18**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.96 (dd, J = 10.7, 4.7 Hz, 1H), 2.84−2.81 (m, 2H), 1.70 (d, J = 6.7 Hz, 3H), 1.07 (d, J = 7.0 Hz, 3H), 0.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.5, 148.0, 146.7, 136.3, 120.0, 118.4, 116.3, 111.2, 111.0, 56.0 (2C), 48.8, 48.4, 46.5, 39.6, 33.3, 18.6, 13.5, 10.3.

Computational Details. The Gaussian 09[32] software package was employed to perform quantum mechanical calculations on the cationic products of the BF_3-mediated Nazarov reaction of each AVK (**14a**−**14l**) via both inward rotation, i.e., cation of type **A**, and outward rotation, i.e., cation of type **B**, and the transition states leading to these products were located. Stationary points were fully optimized in their ground states at the ωB97X-D/6-31+G(d,p) level of theory.[21] Initial calculations at the B3LYP/6-31G(d) level of theory[33] had initially located the same products and transition states, and the intrinsic reaction coordinate method[34] was used to connect those transition states to the corresponding starting material and product minima. Minima and first-order saddle points were characterized by their number of imaginary frequencies following normal-mode vibrational analysis, i.e., 0 and 1, respectively. All geometries and thermodynamic data were obtained from calculations done in the gas phase at 298.15 K and 1.0 atm.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra; Cartesian coordinates and energies. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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