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Brønsted Acid-Mediated Nazarov Cyclization of Vinylallenes

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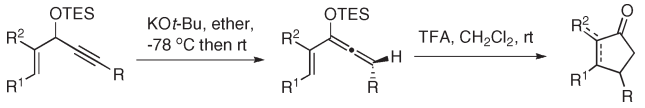
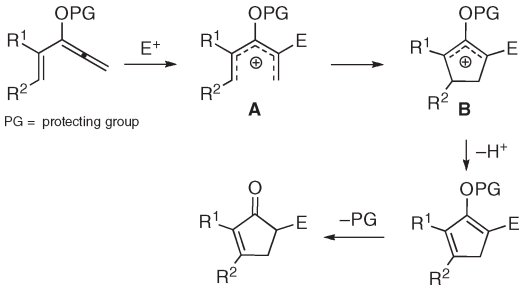


Treatment of siloxy enynes with base leads to the corresponding vinylsiloxyallenes which undergo Nazarov cyclization in the presence of trifluoroacetic acid to provide the cyclized product as a mixture of regioisomers in moderate to good overall yield.

The Nazarov reaction as conventionally practiced converts cross-conjugated dienones into cyclopentenones with Brønsted or Lewis acid activation.[1] As a result of its unique mechanistic features, the Nazarov reaction provides a versatile platform for initiating domino processes;[2] therefore, complex polycarbocycles can be generated in an extremely efficient fashion. Recently, there has been considerable interest in alternative precursors to the key pentadienyl cation intermediate, potentially offering access to unusual substitution patterns or milder conditions.[3] Examples include allenyl vinyl ketones,[3a,b] α-diketones,[3c] vinyldichlorocyclopropanes,[3d] cross-conjugated trienes,[3e] and several transition-metal-catalyzed cycloisomerization approaches.[3f−j] We envisioned another strategy, relying on 3-oxygenated 1,2,4-trienes (vinyl allenes) as the precursors (Scheme 1).

SCHEME 1. Vinyl Allenes as Nazarov Precursors



The notion of activating a vinylallene via epoxidation has been described previously[4] and was recently applied using a 3-alkoxyvinylallene in an elegant and efficient synthesis of (±)-rocaglamide.[5] Transition-metal-catalyzed methods have also been reported.[6] For example, Iwasawa (Pt(II))[6a] and Toste (Au(I))[6b] have described cyclization of simple vinylallenes, and Malacria and co-workers have also reported a clever approach involving Au(I) activation of 3-acetoxyvinylallenes generated in situ from propargyl acetates.[6c,d] We have sought to generalize the process of electrophilic activation. In theory, addition of any electrophile would be expected to occur at the allene central carbon to furnish directly the desired pentadienyl intermediate **A**. Electrocyclization to cyclopentenyl cation **B** and termination in the usual fashion would then provide cyclopentenones, or alternatively, **B** could be interecepted by a variety of traps in an "interrupted Nazarov" reaction. Here, we describe the results of a preliminary study using Brønsted acid activation, in which protonation of readily prepared 3-silyloxyvinylallenes effects their conversion to cyclopentenones under simple and mild conditions.

The proposed strategy required a reliable and efficient method for preparation of the vinylallene substrates. We settled on a straightforward approach employing base-catalyzed isomerization[7] of suitably protected allyl propargyl alcohols **1**, which should be readily available from acetylide addition to enals (Table 1). In the event, a variety of unsaturated aldehydes were subjected to 1,2-addition of lithium acetylides to afford alcohols **1a**−**j** in high yields. The alcohols were then cleanly protected as triethylsilyl ethers[8] **2a**−**j** by

(1) For recent reviews, see: (a) Pellisier, H. *Tetrahedron* **2005**, *61*, 6479–6517. (b) Frontier, A. J.; Collison, C. *Tetrahedron* **2005**, *61*, 7577–7606. (c) Tius, M. A. *Eur. J. Org. Chem.* **2005**, 2193–2206. (d) Nakanishi, W.; West, F. G. *Curr. Opin. Drug Discov.* **2009**, *12*, 732–751.

(2) Recent examples: (a) Janka, M.; He, W.; Haedicke, I. E.; Fronczek, F. R.; Frontier, A. J.; Eisenberg, R. *J. Am. Chem. Soc.* **2006**, *128*, 5312–5313. (b) Rostami, A.; Wang, Y.; Arif, A. M.; Mc Donald, R.; West, F. G. *Org. Lett.* **2007**, *9*, 703–706. (c) Song, D.; Rostami, A.; West, F. G. *J. Am. Chem. Soc.* **2007**, *129*, 12019–12022. (d) Rieder, C. J.; Fradette, R. J.; West, F. G. *Chem. Commun.* **2008**, 1572–1574. (e) Basak, A. K.; Tius, M. A. *Org. Lett.* **2008**, *10*, 4073–4076. For a recent review, see: (f) Grant, T. N.; Rieder, C. J.; West, F. G. *Chem. Commun.* **2009**, 5676–5688.

(3) (a) Banaag, A. R.; Tius, M. A. *J. Org. Chem.* **2008**, *73*, 8133–8141. (b) Marx, V. M.; Cameron, T. S.; Burnell, D. J. *Tetrahedron Lett.* **2009**, *50*, 7213–7216. (c) Bow, W. F.; Basak, A. K.; Jolit, A.; Vicic, D. A.; Tius, M. A. *Org. Lett.* **2010**, *12*, 440–443. (d) Grant, T. N.; West, F. G. *J. Am. Chem. Soc.* **2006**, *128*, 9348–9349. (e) Rieder, C. J.; Winberg, K. J.; West, F. G. *J. Am. Chem. Soc.* **2009**, *131*, 7504–7505. (f) Lin, G.-Y.; Yang, C.-Y.; Liu, R.-S. *J. Org. Chem.* **2007**, *72*, 6753–6757. (g) Sans, R.; Miguel, D.; Rodriguez, F. *Angew. Chem., Int. Ed.* **2008**, *47*, 7354–7357. (h) Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442–1443. (i) Nakanishi, Y.; Miki, K.; Ohe, K. *Tetrahedron* **2007**, *63*, 12138–12148. (j) Abu Sohel, S. M.; Lin, S.-H.; Liu, R.-S. *Synlett* **2008**, 745–750.

(4) (a) Doutheau, A.; Gore, J.; Malacria, M. *Tetrahedron* **1977**, *33*, 2393–2398. (b) Corey, E. J.; Ritter, K.; Yus, M.; Majera, C. *Tetrahedron Lett.* **1987**, *28*, 3547–3550. (c) Hess, B. A. J.; Smentek, L.; Brash, A. R.; Cha, J. K. *J. Am. Chem. Soc.* **1999**, *121*, 5603–5604.

(5) Malona, J. A.; Cariou, K.; Frontier, A. J. *J. Am. Chem. Soc.* **2009**, *131*, 7560–7561.

(6) (a) Funami, H.; Kusama, H.; Iwasawa, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 909–911. (b) Lee, J. H.; Toste, F. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 912–914. (c) Lemiere, G.; Gandon, V.; Cariou, K.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2007**, *9*, 2207–2209. (d) Lemiere, G.; Gandon, V.; Cariou, K.; Hours, A.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2009**, *131*, 2993–3006.

(7) (a) Mantione, R.; Leroux, Y. *Tetrahedron Lett.* **1971**, *12*, 591–592. (b) Tius, M. A.; Stergiades, I. A. *J. Org. Chem.* **1999**, *64*, 7547–7551.

(8) The corresponding triisopropylsilyl ethers could also be prepared in high yields, but the subsequent isomerization step failed to go to completion with the bulkier protecting group.

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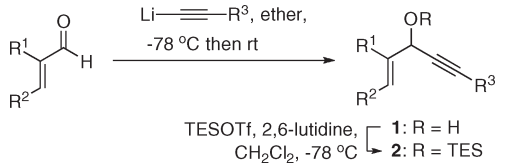
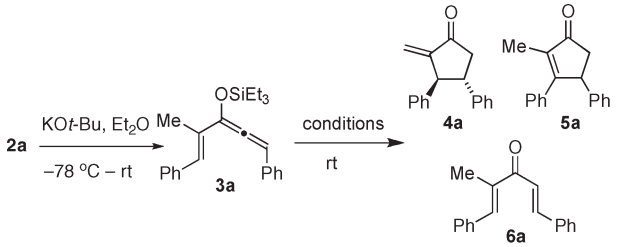
TABLE 1. Preparation of Siloxy Enynes 2[a]



entry	R^1	R^2	R^3	product of step 1 (% yield)[b]	product of step 2 (% yield)[b]
1	Me	Ph	Ph	**1a** (86)	**2a** (96)
2	Me	Ph	*n*-Hex	**1b** (83)	**2b** (99)
3	Me	Ph		**1c** (90)	**2c** (95)
4	Me	Me	Ph	**1d** (91)	**2d** (72)
5	Me	Me	*n*-Hex	**1e** (94)	**2e** (95)
6	Me	Me		**1f** (95)	**2f** (77)
7	Me	$(CH_2)_2$ Ph	Ph	**1g** (91)	**2g** (91)
8		$(CH_2)_4$	Ph	**1h** (82)	**2h** (95)
9		$(CH_2)_4$	*n*-Hex	**1i** (92)	**2i** (94)
10		$(CH_2)_3$		**1j** (98)	**2j** (73)

[a]General procedures for the two steps are given in the Experimental Section. [b]All yields reported are for isolated material after purification.

SCHEME 2. Nazarov Cyclization of 2a



H_3PO_4/CH_3CN	**6a** (63%)
HCl/CH_3CN	complex
$AcOH/CH_2Cl_2$	**6a** (45%)
$HClO_4/CH_3CN$	**5a** (17%)
CF_3CO_2H/CH_2Cl_2	**4a** (51%) + **5a** (47%)

treatment with Et_3SiOTf at low temperature in the presence of 2,6-lutidine.

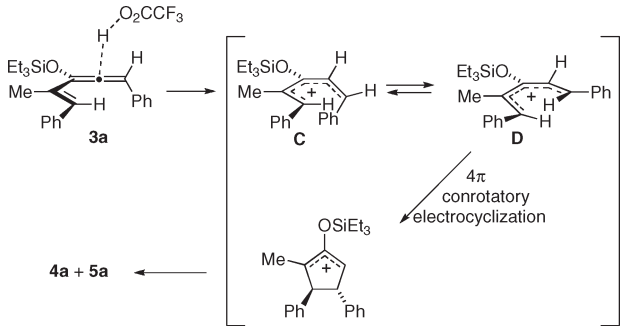
Substrate **2a** was chosen to examine the feasibility of the desired process (Scheme 2). First, isomerization of the enyne to vinylallene **3a** was explored[9] and found to proceed smoothly upon treatment with 1.5 equiv of KO-*t*-Bu at −78 °C, followed by warming to room temperature.[10] While the desired vinylallene **3a** was present as the principal component of the crude reaction mixture, it decomposed during attempted chromatographic purification. Therefore, conditions to effect the Nazarov reaction were evaluated with the unpurified **3a**. A number of Brønsted acids commonly applied to the Nazarov cyclization were tested.[11] Stronger mineral acids such as H_3PO_4 or HCl at room temperature resulted in destruction of **3a** or simple hydrolysis to give dienone **6a**, as was also the case with AcOH.

(9) Yoshizawa, K.; Shioiri, T. *Tetrahedron* **2007**, *63*, 6259–6286.

(10) Use of catalytic amounts (10 mol %) of KO-*t*-Bu resulted in poor conversion and unacceptably slow reactions.

(11) Lewis acids $BF_3 \cdot OEt_2$ and $TiCl_4$ failed to furnish any Nazarov product.

SCHEME 3. Possible Pentadienyl Intermediates



Perchloric acid in CH_3CN did furnish small amounts of the desired cyclopentenone **5a**, but the optimal conditions were trifluoroacetic acid (TFA) in CH_2Cl_2, which afforded a nearly 1:1 mixture of **5a** and methylidenecyclopentanone **4a** in near-quantitative yield.

The trans relative stereochemistry was tentatively assigned to the product **4a** on the basis of 2D NMR analysis of a reduced derivative.[12] Assuming the usual conrotatory electrocyclization pathway, a trans relationship for the phenyl groups demands the intermediacy of (*E*,*E*)-pentadienyl cation **D** (Scheme 3). We presume initial protonation of the allenol silyl ether occurs from the less hindered side, affording (*E*,*Z*)-pentadienyl cation **C**. If this is the case, an isomerization from **C** to **D** must take place prior to electrocyclization.[13]

In order to examine the scope of this process, the remaining substrates **2b**−**j** were then subjected to the standard conditions optimized for **2a** (Table 2). In the event, conversion of enynes **2b**−**j** to the regioisomeric cyclized products **4**/**5** progressed swiftly with moderate to good overall yield (Table 2). In general, the substrate scope was broad with respect to the nature of substituent (R) attached to the alkyne moiety (alkyl, vinyl, or phenyl group). For most acyclic substrates (entries 1−7), the termination of the Nazarov process by proton loss predominantly led to cyclopentenone **5**, in contrast to the preferential formation of exocyclic olefins **4** for six-membered cyclic precursors (entries 8 and 9). In the case of **2j** (entry 10), the remote olefin within the resulting cyclized product isomerized under the acidic reaction conditions to give fully conjugated dienone **7** along with trace amount of hydrolyzed product **6j**. Moreover, **6j** was unreactive under the reaction conditions, indicating that the dienone is not an intermediate in the cyclization process.[14] The relatively low yields of cyclized products seen in the more highly conjugated cases (entries 3, 6, and 10) are consistent with the observations of Tantillo, Sarpong, and co-workers, who found a pronounced reduction in cyclization efficiency of aryl dienyl ketones lacking a substituent at the α position.[15]

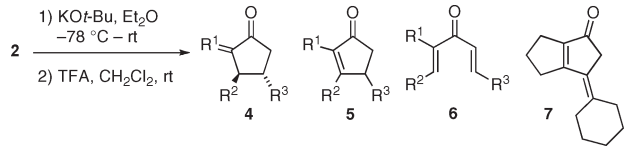
(12) Compound **4a** was reduced under Luche conditions to give the corresponding allylic alcohol as a single diastereomer. See the Supporting Information for the stereochemical assignment based on 2D TROESY NMR data.

(13) Isomerization of (*Z*)-dienones during Nazarov cyclization under Lewis acid conditions has been observed: (a) Denmark, S. E.; Wallace, M. A.; Walker, C. B. *J. Org. Chem.* **1990**, *55*, 5543–5545. (b) Giese, S.; West, F. G. *Tetrahedron* **2000**, *56*, 10221–10228. (c) He, W.; Sun, X.; Frontier, A. J. *J. Am. Chem. Soc.* **2003**, *125*, 12478–12479.

(14) Dienone **6a** did furnish minor amounts of **4a** + **5a** (**6a**:**4a**/**5a** = 9:1) under the standard reaction conditions (TFA/rt/4 h).

(15) Marcus, A. P.; Lee, A. S.; Davis, R. L.; Tantillo, D. J.; Sarpong, R. *Angew. Chem., Int. Ed.* **2008**, *47*, 6379–6383.

TABLE 2. Isomerization and Cyclization of Enynes 2[a]



entry	substrate	R^1	R^2	R^3	product(s) (% yield)[b]
1	**2a**	Me	Ph	Ph	**4a** (51)/**5a** (47)
2	**2b**	Me	Ph	*n*-Hex	**5b** (82)
3	**2c**	Me	Ph		**5c** (35)
4	**2d**	Me	Me	Ph	**4d** (10)/**5d** (30)
5	**2e**	Me	Me	*n*-Hex	**5e** (45)
6	**2f**	Me	Me		**5f** (45)
7	**2g**	Me	$Ph(CH_2)_2$	Ph	**4g** (28)/**5g** (39)
8	**2h**		$(CH_2)_4$	Ph	**4h** (65)/**5h** (14)
9	**2i**		$(CH_2)_4$	*n*-Hex	**4i** (33)/**5i** (20)
10	**2j**		$(CH_2)_3$		**6j** (2)/**7** (28)

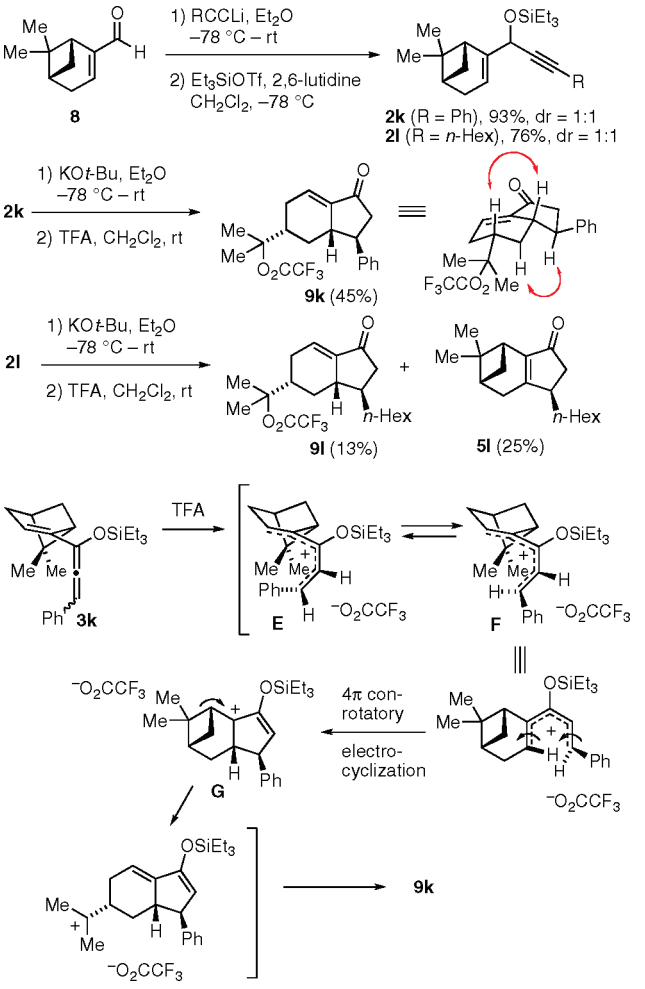
[a]General procedures for the two steps are given in the Experimental Section. [b]All yields reported are for isolated material after purification.

It is notable that all cyclopentenone products **5** were formed with complete regioselectivity in favor of the more substituted alkene isomer. Moreover, no evidence was seen of trapping of the cyclopentenyl cation by trifluoroacetate, in contrast to the recent report by Marx and Burnell.[16] A possible explanation for this difference is a longer lived cyclopentenyl cation intermediate in those cases due to the greater conjugative stabilization.

We also examined two cases in which the pentadienyl system would be part of a rigid, bridged bicyclic system. Related dienone systems had shown significant levels of diastereoselectivity in either silyl-directed Nazarov cyclizations[17] or halide-trapping processes.[18] Enynes **2k** and **2l** were readily prepared from (−)-myrtenal (**8**) via the usual protocol (Scheme 4). In the event, when **2k** was subjected to the typical conditions, the normal cyclized product was not observed. Instead, hydrindenone **9k** was obtained in moderate yield as a single diastereomer, with the relative configuration assigned based upon the indicated TROESY correlations. Likewise, substrate **2l** also furnished hydrindenone **9l**, albeit less efficiently, along with greater amounts of compound **5l** arising from usual eliminative termination.

Products **9k**,**l** are presumed to result from bond cleavage of the strained cyclobutylcarbinyl cation **G** formed after electrocyclization. The resulting isolated tertiary cation would then undergo capture by trifluoroacetate.[19] As with the simpler monocyclic product **4a**, the relative stereochemistry at the two centers in **9** derived from the former termini of the pentadienyl indicates an isomerization of the initially formed (*E*,*Z*)-isomer to the (*E*,*E*) isomer prior to cylization. Surprisingly, the relationship between the tertiary trifluoroacetate side chain and the bridgehead proton indicates that cyclization of this cation occurs *from the same face as the geminal dimethyl bridge*. The exclusive counterclockwise

SCHEME 4. Fragmentation of Bridged Bicyclic Substrates



torquoselectivity of the electrocyclization from that face is presumably preferred over the alternate clockwise rotation, as the latter would move the phenyl substituent into steric conflict with the hindered quaternary carbon of the bridge.

We have found that silyl-protected allyl propargyl alcohols can serve as convenient substrates for Nazarov cyclization, via sequential base-catalyzed isomerization to siloxy vinyl allenes, followed by mild activation with trifluoracetic acid. The modular nature of the substrate synthesis allows for substantial diversity in substitution. Notably, two cases possessing remote stereocenters displayed high levels of diastereoselectivity, as well as an intriguing fragmentation/trapping pathway. Other approaches for electrophilic activation of vinyl allenes, and methods for intercepting the cyclized intermediate, are under current investigation and will be described in due course.

Experimental Section

Representative Acetylide Addition Procedure: (*E*)-2-Methyl-1,5-diphenylpent-1-en-4-yn-3-ol (1a). To a flame-dried round-bottom flask containing a magnetic stirring bar were added phenylacetylene (3.98 mmol, 406 mg) and ether (8 mL) under Ar. The temperature of the solution was dropped to −78 °C. *n*-BuLi (1.60 M solution in hexane, 3.98 mmol, 2.48 mL) was added dropwise, and the reaction mixture was stirred at the same temperature for 30 min. The α-methyl-*trans*-cinnamaldehyde (3.98 mmol, 581 mg) was

(16) Marx, V. M.; Burnell, D. J. *Org. Lett.* **2009**, *11*, 1229–1231.
(17) Mazzola, R. D., Jr.; White, T. D.; Vollmer-Snarr, H. R.; West, F. G. *Org. Lett.* **2005**, *7*, 2799–2801.
(18) White, T. D.; West, F. G. *Tetrahedron Lett.* **2005**, *46*, 5629–5632.
(19) Analogous halide trapping of a fragmented intermediate was observed in the TiX_4-mediated Nazarov cyclization of myrtenal-derived dienones (see ref 18).

added, and the resulting solution was allowed to warm to room temperature. The reaction was quenched with saturated aqueous NH_4Cl and diluted with ether. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to provide pure compound **1a** (850 mg, yield 86%): R_f 0.28 (hexane/EtOAc 4:1); IR (film) 3341 (br), 3081, 3056, 3024, 2981, 2917, 2859, 2201, 1664, 1598, 1573, 1489, 1442, 1381, 1361, 1281, 1070, 1008, 998, 756, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52−7.50 (m, 2H), 7.39−7.30 (m, 7H), 7.29−7.27 (m, 1H), 6.81 (s, 1H), 5.20 (s, 1H), 2.31 (br s, 1H), 2.11 (d, $J = 1.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 136.7, 131.7, 129.0, 128.5, 128.2, 128.1, 127.2, 126.7, 122.4, 88.0, 86.3, 68.7, 14.1; HRMS (EI, M^+) for $C_{18}H_{16}O$ calcd 248.1201, found:*m*/*z* 248.1196.

Representative Silyl Protection: ((*E*)-2-Methyl-1,5-diphenylpent-1-en-4-yn-3-yloxy)triethylsilane (2a). To a flame-dried round-bottom flask containing a magnetic stirring bar were sequentially added hydroxyenyne **1a** (1.06 mmol, 264 mg), CH_2Cl_2 (5 mL), and 2,6-lutidine (3.18 mmol, 0.37 mL) under Ar. The temperature of the solution was dropped to −78 °C. Triethylsilyl trifluoromethanesulfonate (1.59 mmol, 0.36 mL) was added dropwise, and the resulting solution was stirred at the same temperature for 30 min. The reaction mixture was quenched with H_2O and diluted with CH_2Cl_2. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude mixture thus obtained was purified by flash column chromatography (silica gel, 2% EtOAc/hexane) to give pure siloxyenyne **2a** (369 mg, yield 96%): R_f 0.80 (hexane/EtOAc 4:1); IR (film) 3081, 3060, 3026, 2956, 2912, 2876, 2203, 1691, 1665, 1490, 1450, 1238, 1060, 1003, 754, 690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53−7.50 (m, 2H), 7.43−7.35 (m, 7H), 7.29−7.27 (m, 1H), 6.80 (br s, 1H), 5.21 (s, 1H), 2.11 (d, $J = 1.2$ Hz, 3H), 1.16−1.06 (m, 9H), 0.86−0.80 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.5, 137.5, 131.6, 129.0, 128.2, 128.0, 126.5, 125.7, 123.0, 89.2, 85.0, 68.7, 14.1, 6.8, 4.9 (one sp^2 carbon signal is missing due to peak overlap); HRMS (EI, M^+) for $C_{24}H_{30}OSi$ calcd 362.2066, found: *m*/*z* 362.2063.

Representative Alkyne−Allene Isomerization and Nazarov Cyclization: 2-Methylene-3,4-diphenylcyclopentanone (4a) and 2-Methyl-3,4-diphenylcyclopent-2-enone (5a). To a flame-dried round-bottom flask containing a magnetic stirring bar were added siloxy enyne **2a** (0.044 mmol, 16 mg) and ether (4 mL) under Ar. The temperature of the solution was dropped to −78 °C (acetone/dry ice bath). KO-*t*-Bu (0.07 mmol, 7 mg) was added in one portion, and the resulting suspension was stirred vigorously followed by the immediate removal of the cooling bath. Upon consumption of **2a** as determined by thin-layer chromatography, the reaction was quenched with 15% aqueous NH_4Cl and diluted with ether. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated to give the crude siloxyallene **3a** which was used for the next step without further purification. The unpurified **3a** thus obtained was dissolved in CH_2Cl_2 (2 mL) and treated with trifluoroacetic acid (3.0 equiv based on **2a**, 0.13 mmol, 10 μL) at room temperature. After the mixture was stirred for 4 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and diluted with CH_2Cl_2. The separated organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. The crude mixture was purified by flash column chromatography (silica gel, 10% EtOAc/hexane) to provide the desired products **4a** (5.6 mg, yield 51%) and **5a** (5.1 mg, yield 47%). **4a**: R_f 0.61 (hexane/EtOAc 4:1); IR (film) 3085, 3061, 3028, 2925, 2854, 1718, 1601, 1495, 1453, 1119, 1075, 785, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.17 (m, 6H), 7.12−7.07 (m, 4H), 6.22 (dd, $J =$ 3.3, 0.9 Hz, 1H), 5.04 (dd, $J = 3.0$, 0.8 Hz, 1H), 3.96 (ddd, $J =$ 10.6, 3.0, 3.0 Hz, 1H), 3.41 (ddd, $J = 11.2$, 11.2, 7.2 Hz, 1H), 2.91 (ddd, $J = 18.2$, 7.6, 0.8 Hz, 1H), 2.71 (dd, $J = 18.0$, 12.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.7, 149.6, 141.1, 140.9, 128.9, 128.8, 128.8, 127.4, 127.3, 127.2, 120.0, 56.7, 48.9, 45.8; HRMS (EI, M^+) for $C_{18}H_{16}O$ calcd 248.1201, found *m*/*z* 248.1201. **5a**: R_f 0.50 (hexane/EtOAc 4:1); IR (film) 3060, 3027, 2923, 2853, 1698, 1624,1495, 1454, 1443, 1378, 1342, 1076, 761, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27−7.02 (m, 10H), 4.43 (ddq, $J = 7.1$, 2.0, 2.0 Hz, 1H), 3.05 (dd, $J = 19.0$, 7.2 Hz, 1H), 2.44 (dd, $J = 19.0$, 2.2 Hz, 1H), 1.97 (d, $J = 2.0$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 169.1, 142.4, 137.7, 135.3, 128.9, 128.7, 128.3, 128.0, 127.3, 126.7, 47.1, 45.1, 9.9; HRMS (EI, M^+) for $C_{18}H_{16}O$ calcd 248.1201, found *m*/*z* 248.1198.

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Supporting Information Available: Characterization data for **1b**−**l**, **2b**−**l**, **4d**,**g**−**i**, **5b**-**i**,**l**, **6j**, **7**, and **9k**,**l**, stereochemical assignment of **4a** via reduction and derivatization, and copies of NMR spectra for all products and synthetic intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.