

A benzannulation strategy for the synthesis of phenols and heteroaromatic compounds based on the reaction of (trialkylsilyl)vinylketenes with lithium ynolates

Wesley F. Austin, Yongjun Zhang, Rick L. Danheiser*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139, USA

Received 13 August 2007; received in revised form 17 October 2007; accepted 26 October 2007

Available online 3 December 2007

Abstract

(Trialkylsilyl)vinylketenes react with lithium ynolates to generate 3-(oxido)dienylketenes, which undergo rapid 6π -electrocyclization. The ultimate products of this benzannulation are highly substituted resorcinol monosilyl ethers, which are formed via a [1,3] carbon to oxygen silyl group shift. Further transformations of the benzannulation products are described providing efficient access to *ortho*-benzoquinones and benzofuran, benzoxepine, and benzoxocine ring systems.

© 2007 Elsevier Ltd. All rights reserved.

Keywords: (Trialkylsilyl)vinylketenes; Benzannulation; Ynolates; Electrocyclic ring closure

1. Introduction

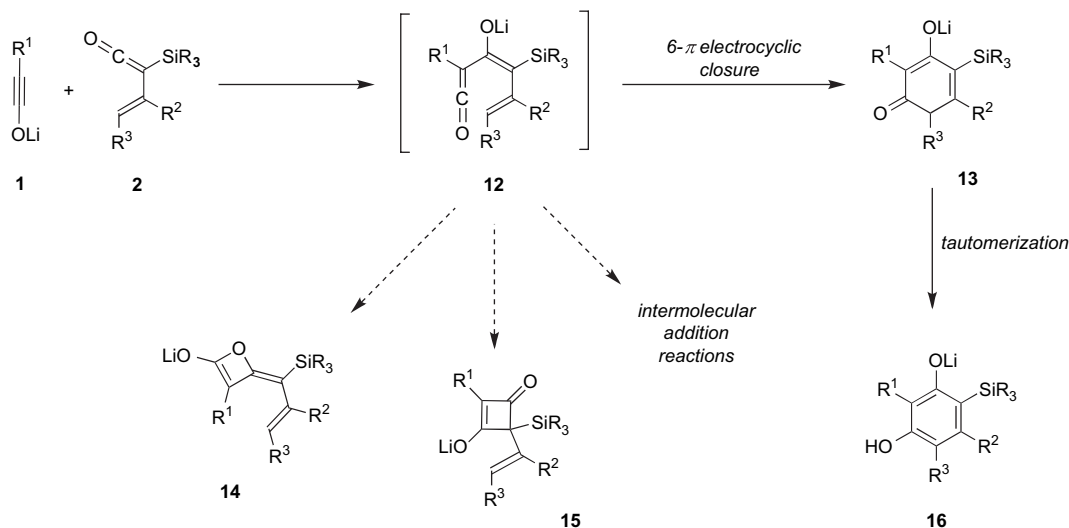
The development of efficient strategies for the synthesis of highly substituted aromatic systems is a problem of considerable importance in organic chemistry. Classically, syntheses of highly substituted benzenoid compounds have most often been achieved by employing linear substitution strategies involving sequential electrophilic substitution and metalation–alkylation reactions. Frequently, however, a more effective approach involves the application of benzannulation methods: convergent strategies in which the aromatic ring system is assembled from two or more precursors in a single step, with all (or most) substituents in place. Benzannulation strategies enjoy significant advantages over conventional linear substitution strategies, especially when applied to the preparation of highly substituted target molecules. For example, benzannulation routes generally avoid the regiochemical ambiguities associated with aromatic substitution reactions, and their intrinsic convergent character facilitates the efficient assembly of highly substituted aromatic compounds that

would require long, multistep routes using classical substitution methodology.

In this paper we report full details of our studies of a benzannulation strategy based on the reaction of lithium ynolates with (trialkylsilyl)vinylketenes ('TAS-vinylketenes').¹ The utility of vinylketenes² in organic synthesis is well-established. Research in our laboratory has shown that [2+2] cycloadditions of vinylketenes can serve as triggering steps in powerful 'pericyclic cascade' strategies for the synthesis of six- and eight-membered carbocyclic compounds.^{3,4} In related studies, we have demonstrated that (trialkylsilyl)vinylketenes are remarkably stable ketenes, which exhibit reactivity complementary to other vinylketenes in many useful synthetic transformations. Silyl substituents⁵ suppress the tendency of vinylketenes to undergo dimerization and [2+2] cycloaddition, allowing them to express their underlying reactivity as electron-rich conjugated dienes in Diels–Alder reactions⁶ and as reactive carbonyl compounds in [4+1] annulations leading to five-membered rings.^{7,8} Herein we report the reaction of TAS-vinylketenes with lithium ynolates in a benzannulation process that provides access to highly substituted phenols and several classes of oxygen heteroaromatic compounds (Scheme 1).

* Corresponding author. Tel.: +1 617 253 1842; fax: +1 617 252 1504.

E-mail address: danheiser@mit.edu (R.L. Danheiser).



Scheme 4. Proposed benzannulation reaction pathway and potential side reactions.

closure over alternative cyclization pathways and intermolecular condensation reactions. The possibility that the cyclohexadiene intermediate **13** might form via a concerted [4+2] cycloaddition of the ynoate to the ketene cannot be excluded; however, previous research in our laboratory has demonstrated that TAS-vinylketenes behave as electron-rich dienes in Diels–Alder cycloadditions and generally require electron-deficient dienophiles for successful reaction.⁶ Consistent with this is the observation that no reaction was observed to take place upon heating a solution of TAS-vinylketene **7a** with siloxy alkyne **10f** in toluene at reflux for 8 h.

The initial investigation of the feasibility of the benzannulation was conducted using TAS-vinylketene **7b** and the lithium ynoate derived from siloxy alkyne **10a**. Cleavage of the silyl ether took place smoothly upon exposure of the siloxy alkyne to 1 equiv of methyllithium in THF at rt, with TLC analysis indicating complete consumption of the silyl ynoate within 3.5 h. Addition of ketene **7b** then resulted in a gold-colored mixture, and TLC analysis showed the formation of a single new aromatic product, which was obtained in 67% yield following purification by silica gel chromatography. Interestingly, however, ¹H NMR data for this compound was not consistent with that expected for the resorcinol derivative with a hexa-substituted benzene ring that would result from protonation of a benzannulation product of type **16**. In particular, two downfield singlets were observed at 6.19 and 4.71 ppm, with only the latter exhibiting exchange with D₂O. Further analysis suggested that a migration of the trialkylsilyl group from carbon to oxygen had taken place, and the benzannulation product was in fact the silyl ether **33** (Table 1, entry 1). Additional support for this structure was obtained by NOE studies of the related annulation product **31** (Fig. 1), which allowed unequivocal assignment of the regiochemistry as that shown.

Evidence that the silyl ether benzannulation products are formed via an intramolecular silyl shift was obtained by the crossover experiment summarized in Scheme 5. Thus, reaction

of a 1:1 mixture of TAS-vinylketenes **7b** and **17** with 1 equiv of ynoate **18** led to the formation of two phenolic products assigned by NMR and GC–MS analysis as **19** and **20**. Neither of the phenols **21** and **22** that would result from intermolecular silyl group transfer could be detected in the crude product of the reaction.

As outlined in Scheme 6, we propose that the observed silyl group migration takes place via a 1,3 carbon → oxygen shift involving a 6-silyl-2,4-cyclohexadienone intermediate of type **24**. 1,3-Silyl shifts in α -silyl ketones to form silyl enol ethers are well known processes,¹⁷ and related rearrangements involving silylcyclohexadienones have been observed in our laboratory^{6b} and others.¹⁸ We speculate that **24** is generated by tautomerization of **23**, which is itself derived from the initial electrocyclization product **13** via tautomerization to **16** followed by a series of (reversible) proton transfer steps. The small difference in $\text{p}K_{\text{a}1}$ and $\text{p}K_{\text{a}2}$ values for the hydroxyl groups in resorcinol (9.2 and 10.9 in water¹⁹) suggests that interconversion of the monolithium salts **16** and **23** may proceed via disproportionation to form a mixture of the corresponding resorcinol and its dilithium derivative. Once **23** forms, tautomerization can produce the 6-silyl-2,4-cyclohexadienone **24**, which then aromatizes via irreversible 1,3-silyl shift.

Table 1 delineates the scope of the TAS-vinylketene-ynoate benzannulation reaction. Optimal conditions were found to involve the generation of the ynoate using 1 equiv of methyllithium; low yields of benzannulation products were obtained when TBAF, TBAT, or KOEt²⁰ was employed in place of MeLi for the reaction. Addition of the ynoate to TAS-vinylketenes was observed to take place within 30–60 min at rt, and the benzannulation products **26–36** were obtained in fair to good yield following aqueous workup and chromatographic purification. Direct analysis of the reaction mixture prior to workup showed the presence of only silyl ether benzannulation products, suggesting that the silyl shift is not occurring during isolation or purification. As noted above, direct reaction of siloxy alkynes with TAS-vinylketenes did not take place at 25 °C or

Table 1
Benzannulation via reaction of TAS-vinylketenes with lithium ynolates

Entry	Alkyne	Ketene	Product	Yield ^a (%)	Entry	Alkyne	Ketene	Product	Yield ^a (%)
1	10f	7a		62	7	10d	7c		37
2	10b	7a		65	8	10a	7b		67–71
3	10j	7a		55	9	10h	7b		43
4	10i	7a		30	10	11	7b		44–48
5	10c	7c		46	11	10c	7d		44–46
6	10e	7c		68–70	12	10k	7a	See text	

^a Isolated yield of products purified by column chromatography.

at elevated temperatures, and attempts to promote benzannulation with Lewis or Brønsted acids (ZnI_2 , TiCl_4 , AgNTf_2 , HNTf_2) were unsuccessful, resulting only in complex mixtures of products.

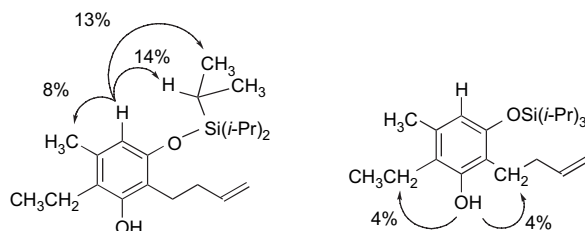
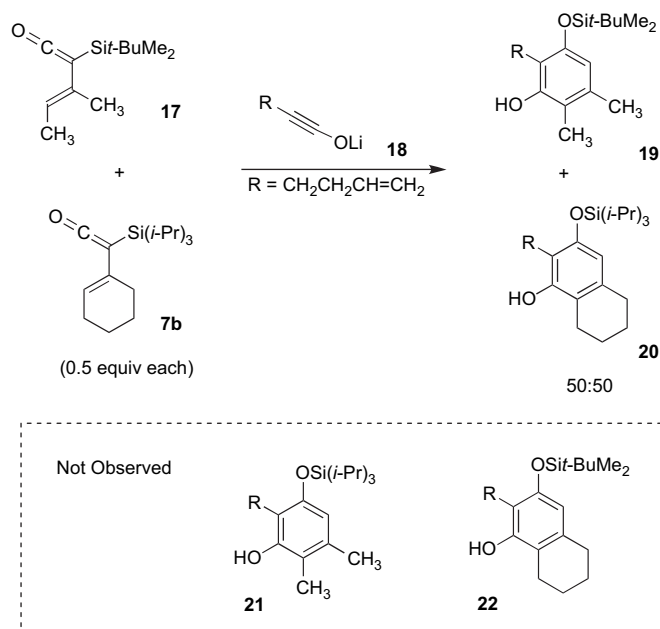


Figure 1. NOE studies on benzannulation product **31**.

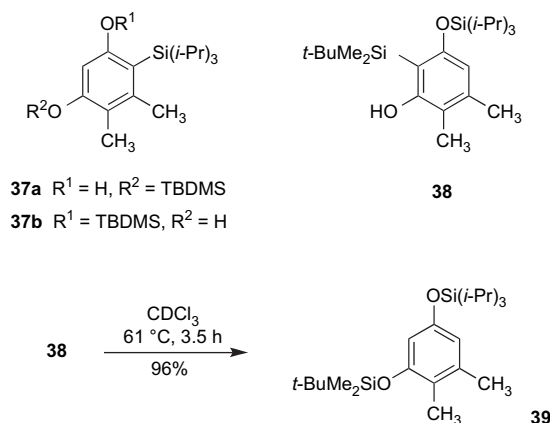
A wide variety of siloxy alkynes participate in the benzannulation (Table 1). Primary, secondary, and tertiary alkyl substituents on the siloxy alkyne are all well tolerated, and alkenyl and aryl derivatives react albeit in somewhat diminished yield. A low yield of the desired benzannulation product was obtained in the case of the allyl-substituted acetylene **10g**, apparently due to competitive metalation at the methylene carbon by MeLi during the ynone generation step.²¹ This problem is easily circumvented, however, by substituting the TBDMS ynone ether **11** for the TIPS derivative **10g** as the ynone precursor. Cleavage of this more reactive siloxy alkyne is complete within minutes, and upon reaction with TAS-vinylketene **7b** the desired benzannulation product **35** is obtained in good yield. In general, however, the use of triisopropylsiloxy alkynes is



Scheme 5. Crossover experiment.

preferred due to their increased stability toward purification and storage. With respect to the TAS-vinylketene annulation partner, the only limitation identified to date is that TAS-aryl and TAS-heteroarylketenes do not undergo benzannulation, producing only complex mixtures of unidentifiable products. In these cases the 6π electrocyclic ring closure would require disruption of aromaticity, which may retard the rate of this cyclization step and permit the alternative processes outlined in Scheme 4 to become competitive.

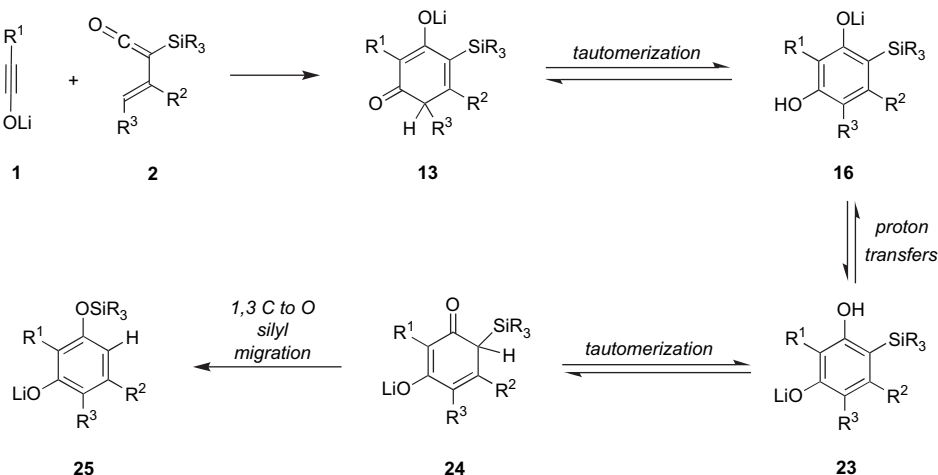
Interesting results were obtained when the *tert*-butyldimethylsilyl-substituted ynone derived from **10k** was employed in the benzannulation. In this case a 3:2 mixture of two phenols was produced in a combined yield of ca. 40–60%.²² Spectroscopic analysis identified the minor product as **38** and the major product as either **37a** or the isomeric silyl ether **37b** (Scheme 7). Unfortunately, to date we have been unable to unambiguously distinguish between these two structures for the major product.

Scheme 7. Results of benzannulation of TAS-vinylketene **7e** with the ynone derived from **10k**.

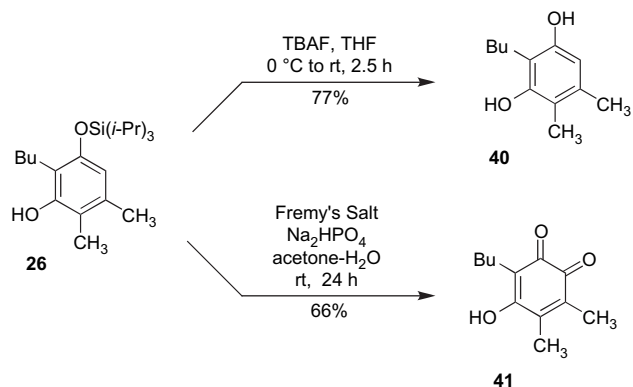
Upon heating in chloroform or benzene, **38** underwent carbon to oxygen 1,3-silyl shift in near quantitative yield to afford **39**, the structure of which was confirmed by desilylation to produce the corresponding resorcinol.^{23,24} In contrast, **37** was largely unchanged after heating in toluene at reflux for 14 h. We believe that annulation product **38** is generated via the usual mechanism as outlined in Scheme 6 (where $R^1 = \text{tert-butyldimethylsilyl}$), while **37a** and **37b** can arise from tautomeric forms of intermediates **16** and **23**, respectively.

2.3. Transformations of benzannulation products

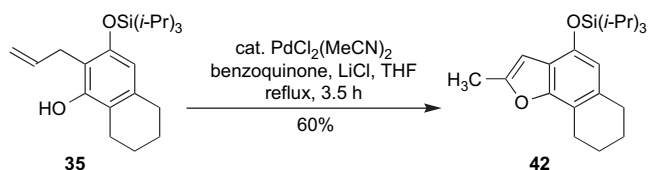
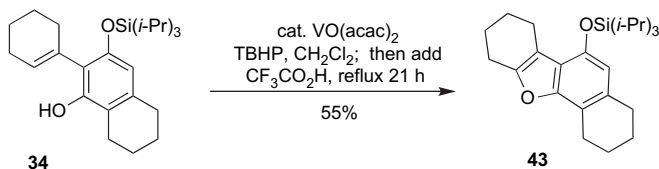
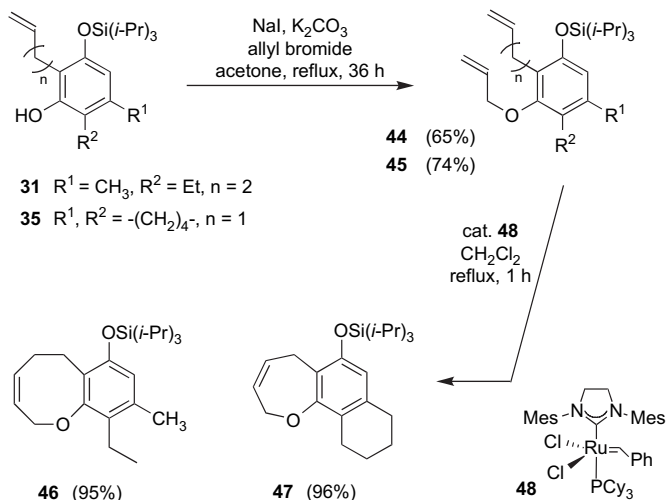
The regiocontrolled benzannulation strategy described herein provides access to *ortho*-substituted phenols that can participate in a variety of useful synthetic transformations. Scheme 8 outlines several straightforward functional group manipulations. Desilylation of **26** is readily accomplished with TBAF to afford the expected resorcinol, and oxidation of **26** with Fremy's salt furnishes the *ortho*-quinone **41** in good yield. Of particular synthetic utility are benzannulation products bearing unsaturated *ortho* substituents such as **31**, **32**, **34**, and **35**, which are useful substrates in cyclizations leading to a variety of benzofused oxygen heterocycles.²⁵



Scheme 6. Mechanism of silyl shift in benzannulation.

Scheme 8. Desilylation and oxidation of benzannulation product **26**.

For example, exposure of the *ortho*-allyl phenol **35** to catalytic $\text{PdCl}_2(\text{MeCN})_2$ in the presence of LiCl and benzoquinone provides tetrahydronaphthofuran **42** in good yield (Scheme 9),²⁶ while the vinyl-substituted benzannulation product **34** can be converted to the tetracyclic benzofuran **43** using the general method of Lattanzi (Scheme 10).²⁷

Scheme 9. Palladium-catalyzed cyclization of benzannulation product **35**.Scheme 10. Synthesis of benzofuran from benzannulation product **34**.

Scheme 11. Synthesis of oxygen heterocycles via ring closing metathesis.

A variety of benzofused oxygen heterocyclic systems are also available from the benzannulation products through the application of ring closing metathesis.²⁸ Scheme 11 illustrates this strategy as applied to the synthesis of the benzoxocine **46** and benzoxepine **47**.

3. Conclusions

We have shown that TAS-vinylketenes react with lithium ynolates in a regiocontrolled benzannulation process that provides efficient access to highly substituted phenols. In conjunction with transition-metal catalyzed cyclization reactions, this strategy can be employed for the synthesis of a variety of benzofused oxygen heterocycles, including benzofurans, benzo[b]oxocines, and benzo[b]oxepines.

4. Experimental

4.1. General

All reactions were performed in flame-dried or oven-dried glassware under a positive pressure of argon. Reaction mixtures were stirred magnetically unless otherwise indicated. Air- and moisture-sensitive liquids and solutions were transferred by syringe or cannula and were introduced into reaction vessels through rubber septa. Reaction product solutions and chromatography fractions were concentrated by rotary evaporation at ca. 20 mm Hg and then at ca. 0.1 mm Hg (vacuum pump) unless otherwise indicated. Thin layer chromatography was performed on Merck precoated glass-backed silica gel 60 F-254 0.25 mm plates. Column chromatography was performed on Silicycle silica gel 60 (230–400 mesh) or Sorbent silica gel 60A (32–63 μm).

4.2. Materials

Commercial grade reagents and solvents were used without further purification except as indicated below. Triisopropylsilyl trifluoromethanesulfonate, 1,1,1,3,3,3-hexamethyldisilazane, benzene, and diisopropylethylamine were distilled under argon from calcium hydride. Dichloromethane, diethyl ether, and tetrahydrofuran were purified by pressure filtration through activated alumina. Toluene was purified by pressure filtration through activated alumina and copper(II) oxide. Anhydrous *tert*-butyl hydroperoxide in toluene was prepared from the aqueous solution as described by Sharpless.²⁹ Methylolithium was obtained from either Aldrich Chemical Co. (1.6 M in Et_2O , 0.05 M halide content) or Alfa Aesar (1–2 M in Et_2O , 'low halide'). In some cases decreased yields were observed when aged methylolithium was used in the benzannulation. Methylolithium and *n*-butyllithium were titrated according to the Watson–Eastham method using BHT in THF with 1,10-phenanthroline as an indicator.³⁰ Previously reported methods were employed for the preparation of TAS-vinylketenes **7a**,^{6b} **7b**,^{6b} **7c**,¹ and **7d**.¹ Several known siloxy alkynes were prepared according to the previously described procedures either using the method of Kowalski (**10a**,¹²

10b,³¹ **10c**,¹ **10d**,¹²) or the method of Julia (**10e**,³² **10f**,³³ **10g**,¹ **10h**,¹ **10i**,¹⁴ **10j**,³⁴ and **11**,¹ the preparation of the new siloxy alkyne **10k** is described below.

4.3. Instrumentation

Melting points were determined with a Fisher–Johns melting point apparatus and are uncorrected. Infrared spectra were obtained using a Perkin–Elmer 2000 FT-IR spectrophotometer. ¹H NMR and ¹³C NMR spectra were measured with a Varian Inova 500 MHz spectrometer or a Varian 300 MHz spectrometer. ¹H NMR chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane (with the CHCl₃ peak at 7.27 ppm or the residual benzene peak at 7.16 ppm used as a standard). ¹³C NMR spectra chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane (with the central peak of CDCl₃ at 77.23 ppm or the C₆D₆ peak at 128.06 ppm used as a standard). High resolution mass spectra (HRMS) were measured on a Bruker Daltonics APEX II 3 T Fourier transform mass spectrometer or a Bruker Daltonics APEX IV 4.7 T Fourier transform ion cyclotron resonance mass spectrometer.

4.4. 2-(*tert*-Butyldimethylsilyl)-(E)-2-(1-methyl-1-propenyl)ketene (**17**)

A 50-mL, two-necked, round-bottomed flask equipped with a rubber septum, glass stopper, and argon inlet adapter was charged with a solution of 1-diazo-3-methyl-3-penten-2-one^{9a} (0.500 g, 4.0 mmol) in 20 mL of 1:1 Et₂O–hexanes and cooled at 0 °C while *i*-Pr₂EtN (0.71 mL, 0.53 g, 4.1 mmol) was added dropwise over 1 min. After 3 min, *t*-BuMe₂SiOTf (0.93 mL, 1.1 g, 4.1 mmol) was added dropwise over 1 min, and the resulting solution was allowed to slowly warm to 10 °C over 2.5 h, and then stirred at rt for an additional 30 min. The reaction mixture was filtered through Celite with the aid of 10 mL of hexanes, and the filtrate was concentrated to afford 1.048 g of an orange oil. Column chromatography on 60 g of silica gel (elution with 2% EtOAc–1% Et₃N–hexanes) provided 0.716 g (75%) of 1-(*tert*-butyldimethylsilyl)-1-diazo-3-methyl-1-(E)-3-penten-2-one as a yellow oil: IR (neat) 2929, 2858, 2066, 1615 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.13 (qq, *J*=6.9, 1.4 Hz, 1H), 1.81 (app quint, *J*=1.1 Hz, 3H), 1.76 (dq, *J*=6.7, 1.1 Hz, 3H), 0.94 (s, 9H), 0.23 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 196.4, 136.7, 130.5, 51.6, 26.9, 19.3, 13.9, 13.3, –6.0. A solution of this silylated diazo ketone (0.693 g, 2.91 mmol) in 30 mL of benzene was distributed evenly between two 30-cm quartz tubes fitted with rubber septa. A second rubber septum (inverted) was secured with vinyl tape to each tube to ensure a good seal, and the reaction mixtures were degassed (three freeze–pump–thaw cycles at –196 °C, <0.5 mm Hg) and then irradiated with 300 nm light in a Rayonet reactor for 3 h. The resulting solutions were combined and concentrated at reduced pressure to afford 0.513 g of a yellow oil. Column chromatography on 30 g of silica gel (elution with hexanes) provided 0.393 g (64%) of ketene **17** as a yellow oil: IR (neat) 2930, 2859, 2077, 1647 cm⁻¹; ¹H NMR

(300 MHz, CDCl₃) δ 5.22 (qq, *J*=7.0, 1.3 Hz, 1H), 1.80 (app quint, *J*=1.1 Hz, 3H), 1.62 (dq, *J*=6.7, 1.0 Hz, 3H), 0.93 (s, 9H), 0.18 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 184.6, 124.1, 120.3, 27.0, 25.3, 19.3, 19.2, 14.2, –4.3.

4.5. 2-*tert*-Butyldimethylsilyl-1-(triisopropylsiloxy)-ethyne (**10k**)

A 100-mL, two-necked, round-bottomed flask equipped with a rubber septum and argon inlet adapter was charged with a solution of *tert*-butyldimethylsilylacetylene (0.86 mL, 0.65 g, 4.6 mmol) in 15 mL of THF and cooled at –78 °C while 5.5 mL of LiHMDS solution (1.0 M in THF, 5.5 mmol)³⁵ was added rapidly dropwise over 30 s. A 50-mL, two-necked, round-bottomed flask equipped with a rubber septum and argon inlet adapter was charged with a solution of *tert*-butyl hydroperoxide (4.0 M in toluene, 1.4 mL, 5.6 mmol) in 10 mL of THF and cooled at –78 °C while 6.0 mL of LiHMDS solution (1.0 M in THF, 6.0 mmol) was added rapidly dropwise over 30 s. The resulting solution was transferred into the solution of lithium acetylide via cannula over 3 min, the dry ice–acetone bath was replaced with an ice–water bath, and the reaction mixture was stirred for 2.5 h at 0 °C. The reaction mixture was then recooled to –78 °C, and TIPSOTf (1.6 mL, 1.8 g, 6.0 mmol) was added in one portion. The resulting mixture was stirred for 45 min at –78 °C and then at 0 °C for 45 min. The mixture was recooled to –78 °C, diluted with 50 mL of hexanes, and then poured into a separatory funnel containing 40 mL of satd aqueous NaHCO₃ solution. The aqueous phase was separated and extracted with two 25-mL portions of hexanes, and the combined organic phases were washed with 75 mL of water and 75 mL of satd aqueous NaCl solution, dried over Na₂SO₄, filtered, and concentrated (0.25 mm Hg, 2 h) to yield 1.549 g of an orange oil. Bulb-to-bulb distillation (105–110 °C oven temperature, 0.25 mm Hg) provided 0.937 g (65%) of siloxy alkyne **10k** as a colorless oil with spectral characteristics identical to those previously reported:³⁶ IR (neat) 2184 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 1.20–1.30 (m, 3H), 1.13 (d, *J*=6.8 Hz, 18H), 0.90 (s, 9H), 0.03 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 107.9, 27.8, 26.4, 17.5, 17.0, 12.1, –3.6.

4.6. Benzannulation

Experimental procedures and characterization data for benzannulation products **26**, **27**, **30**, **31**, **33**, **34**, and **36** have been reported previously.¹

4.6.1. General procedure: illustrated with preparation of 2-(3-propenyl)-5,6,7,8-tetrahydro-3-(triisopropylsiloxy)-1-naphthol (**35**)

A 25-mL, two-necked, round-bottomed flask equipped with a rubber septum and argon inlet adapter was charged with siloxy alkyne **10g** (0.890 g, 4.53 mmol) and 6 mL of THF. MeLi solution (1.53 M in Et₂O, 3.0 mL, 4.6 mmol) was added dropwise via syringe over 10 s, and the resulting solution was stirred at rt for 30 min. A solution of ketene **7b** (1.267 g, 4.551 mmol) in 3 mL of THF was added via cannula in one

portion (the flask was rinsed with 1 mL of THF), and the resulting solution was stirred for an additional 70 min. The reaction mixture was poured into 20 mL of satd aqueous NH_4Cl solution, the aqueous phase was separated and extracted with two 10-mL portions of Et_2O , and the combined organic phases were washed with 20 mL of water and 20 mL of satd NaCl solution, dried over MgSO_4 , filtered, and concentrated to afford 2.034 g of a yellow oil. Column chromatography on 100 g of silica gel (25% benzene–hexanes) provided 0.788 g (48%) of phenol **35** as a yellow oil: IR (neat) 3550, 3077, 2942, 2866, 1618, 1578, 1495, 1426 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.23 (s, 1H), 6.00 (ddt, $J=17.2$, 10.0, 6.2 Hz, 1H), 5.20 (app dq, $J=17.3$, 1.7 Hz, 1H), 5.12 (app dq, $J=9.9$, 1.7 Hz, 1H), 5.01 (s, 1H), 3.51 (app dt, $J=6.2$, 1.6 Hz, 2H), 2.67 (t, $J=6.1$ Hz, 2H), 2.58 (t, $J=6.1$ Hz, 2H), 1.71–1.88 (m, 4H), 1.25–1.39 (m, 3H), 1.15 (d, 7.2 Hz, 18H); ^{13}C NMR (75 MHz, CDCl_3) δ 153.3, 151.9, 137.0, 136.5, 116.3, 115.7, 112.5, 110.8, 31.8, 29.9, 28.6, 23.7, 22.8, 18.3, 13.3; HRMS-ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{36}\text{O}_2\text{Si}$, 383.2377; found, 383.2380.

4.6.2. 5,6-Dimethyl-2-*tert*-butyl-3-(*triisopropylsiloxy*)phenol (**28**)

Reaction of siloxy alkyne **10j** (0.198 g, 0.778 mmol) with MeLi solution (1.63 M in Et_2O , 0.49 mL, 0.80 mmol) and ketene **7a** (0.200 g, 0.792 mmol) in 5 mL of THF according to the general procedure and purification by column chromatography on 20 g of silica gel (elution with 2% EtOAc–hexanes) provided 0.180 g of a yellow oil. Further purification on a column of 20 g silica gel (elution with 25% benzene–hexanes) afforded 0.151 g (55%) of phenol **28** as a pale yellow oil: IR (neat) 3622, 2947, 2868, 1610, 1567, 1484 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.22 (s, 1H), 5.13 (s, 1H), 2.17 (s, 3H), 2.07 (s, 3H), 1.57 (s, 9H), 1.37 (sept, $J=7.5$ Hz, 3H), 1.15 (d, $J=7.5$ Hz, 18H); ^{13}C NMR (75 MHz, CDCl_3) δ 154.2, 153.8, 134.8, 121.5, 115.6, 114.3, 36.7, 32.5, 20.8, 18.6, 13.9, 11.9; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{38}\text{O}_2\text{Si}$, 351.2714; found, 351.2719.

4.6.3. 5,6-Dimethyl-2-phenyl-3-(*triisopropylsiloxy*)phenol (**29**)

Reaction of siloxy alkyne **10i** (0.200 g, 0.729 mmol) with MeLi solution (1.63 M in Et_2O , 0.46 mL, 0.75 mmol) and ketene **7a** (0.1850 g, 0.733 mmol) in 5 mL of THF according to the general procedure and purification by column chromatography on 15 g of silica gel (elution with 20% benzene–hexanes) afforded 0.080 g (30%) of phenol **29** as a pale yellow oil: IR (neat) 3552, 2942, 2867, 1621, 1570, 1463 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.42–7.49 (m, 2H), 7.32–7.39 (m, 3H), 6.36 (s, 1H), 4.97 (s, 1H), 2.26 (s, 3H), 2.15 (s, 3H), 1.01–1.14 (m, 3H), 0.92 (d, $J=7.5$ Hz, 18H); ^{13}C NMR (75 MHz, CDCl_3) δ 151.5, 151.0, 137.4, 134.0, 131.4, 131.4, 129.2, 129.2, 128.0, 117.4, 115.1, 112.4, 20.6, 18.1, 13.0, 11.7; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{34}\text{O}_2\text{Si}$, 371.2401; found, 371.2412.

4.6.4. 6-Ethyl-5-methyl-2-[(1*E*)-2-phenylethenyl]-3-(*triisopropylsiloxy*)phenol (**32**)

Reaction of siloxy alkyne **10d** (0.226 g, 0.752 mmol) with MeLi solution (1.50 M in Et_2O , 0.50 mL, 0.75 mmol) and ketene **7c** (0.200 g, 0.750 mmol) in 5 mL of THF according to the general procedure and purification by column chromatography on 15 g of silica gel (gradient elution with 25–38% benzene–hexanes) afforded 0.111 g (37%) of phenol **32** as a pale yellow oil: IR (neat) 3552, 2942, 2867, 1621, 1570, 1463 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.50 (d, $J=7.7$ Hz, 2H), 7.37 (t, $J=7.7$ Hz, 2H), 7.31 (d, $J=17.1$ Hz, 1H), 7.25–7.29 (m, 1H), 7.03 (d, $J=17.1$ Hz, 1H), 6.28 (s, 1H), 5.58 (s, 1H), 2.64 (q, $J=7.5$ Hz, 2H), 2.26 (s, 3H), 1.29 (sept, $J=7.6$ Hz, 3H), 1.15 (t, $J=7.6$ Hz, 3H), 1.11 (d, $J=7.4$ Hz, 18H); ^{13}C NMR (75 MHz, CDCl_3) δ 152.0, 151.6, 137.5, 136.4, 131.3, 128.6, 127.4, 126.1, 122.7, 121.5, 113.3, 112.5, 19.5, 19.4, 18.0, 13.7, 12.9; HRMS-EI (m/z): M^+ calcd for $\text{C}_{26}\text{H}_{38}\text{O}_2\text{Si}$, 410.2636; found, 410.2646.

4.6.5. 5-(*tert*-Butyldimethylsiloxy)-3,4-dimethyl-2-(*triisopropylsilyl*)phenol (**37a**) or 5-(*tert*-butyldimethylsiloxy)-2,3-dimethyl-4-(*triisopropylsilyl*)phenol (**37b**) and 2-(*tert*-butyldimethylsilyl)-5,6-dimethyl-3-(*triisopropylsiloxy*)phenol (**38**)

Reaction of siloxy alkyne **10k** (0.250 g, 0.800 mmol) with MeLi solution (1.63 M in Et_2O , 0.50 mL, 0.82 mmol) and ketene **7a** (0.205 g, 0.812 mmol) in 5 mL of THF according to the general procedure provided 0.501 g of orange oil. NMR analysis of this material indicated the presence of two aromatic products **37** and **38** in a ratio of 66:34 and an estimated combined yield of 40–60%. Pure samples of each compound could not be obtained without significant losses due to the presence of impurities with similar chromatographic properties and the fact that both compounds underwent partial decomposition upon attempted purification by chromatography under a variety of conditions. A pure sample of **38** was obtained by the following procedure. Column chromatography on 20 g of silica gel deactivated with acetone and triethylamine (elution with 5% EtOAc–1% Et_3N –hexanes) provided 0.120 g of a yellow oil, which was applied to the top of a column of 5 g of acetone-deactivated silica gel and eluted with 0–1% EtOAc–hexanes to yield 0.047 g (14%) of phenol **38** as a white powder, mp 92–95 °C: IR (CH_2Cl_2) 3603, 3053, 2948, 2948, 2868, 1601, 1469 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 6.25 (s, 1H), 4.96 (s, 1H), 2.21 (s, 3H), 2.06 (s, 3H), 1.42 (sept, $J=7.6$ Hz, 3H), 1.15 (d, $J=7.6$ Hz, 18H), 0.95 (s, 9H), 0.40 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 160.3, 160.1, 139.5, 113.7, 112.6, 108.5, 27.5, 20.9, 18.8, 18.6, 14.0, 11.5, –0.9; HRMS-ESI (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{44}\text{O}_2\text{Si}_2$, 409.2953; found, 409.2957. A pure sample of **37** could not be obtained, but a sample of sufficient purity for identification of NMR characteristics was obtained by the following procedure. The crude product of another run of the benzannulation was first partially purified by column chromatography on 20 g of silica gel deactivated with acetone and triethylamine (elution with 5% EtOAc–1%

Et₃N–hexanes) to afford 0.133 g of a red oil. This material was dissolved in 10 mL of Et₂O, washed with five 5-mL portions of satd aqueous NH₄Cl solution, dried over MgSO₄, filtered, and concentrated to afford 0.069 g of a sample of the major benzannulation product assigned as either **37a** or **37b** (ca. 80% purity) as a yellow oil: ¹H NMR (500 MHz, CDCl₃) δ 6.20 (s, 1H), 4.87–5.00 (br s, 1H), 2.31 (s, 3H), 2.08 (s, 3H), 1.66 (sept, *J*=7.5 Hz, 3H), 1.09 (d, *J*=7.5 Hz), 1.00 (s, 9H), 0.27 (s, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 160.1, 154.8, 146.8, 117.7, 115.7, 104.3, 27.6, 23.1, 20.4, 19.3, 14.5, 12.1, –2.7.

4.7. Transformations of annulation products

4.7.1. 4,5-Dimethyl-3-*tert*-butyldimethylsiloxy-1-triisopropylsiloxy-benzene (**39**)

A 5-mm NMR tube was charged with a solution of phenol **38** (0.026 g, 0.064 mmol) in 0.70 mL of CDCl₃. The reaction mixture was heated at reflux for 3.5 h then allowed to cool and concentrated to yield 0.025 g (96%) of **39** as a pale yellow oil: IR (neat) 2945, 2866, 1603, 1473, 1333 cm^{–1}; ¹H NMR (CDCl₃, 500 MHz) δ 6.35 (d, *J*=2.4 Hz, 1H), 6.22 (d, *J*=2.4 Hz, 1H), 2.18 (s, 3H), 2.04 (s, 3H), 1.22 (m, 3H), 1.10 (d, *J*=7.3 Hz, 18H), 1.01 (s, 9H), 0.19 (s, 6H); ¹³C NMR δ 154.6, 154.3, 139.0, 120.5, 115.3, 108.9, 26.5, 21.2, 19.0, 18.7, 13.4, 12.6, –3.6; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₂₃H₄₄O₂Si₂, 409.2953; found, 409.2959.

4.7.2. 2-Butyl-5,6-dimethylresorcinol (**40**)

A 10-mL, two-necked, round-bottomed flask equipped with a rubber septum and argon inlet adapter was charged with a solution of phenol **26** (0.200 g, 0.570 mmol) in 2 mL of THF and stirred at 0 °C while TBAF solution (1.0 M in THF, 0.85 mL, 0.85 mmol) was added. The reaction mixture was allowed to slowly warm to rt over 2.5 h, and then partitioned between 5 mL Et₂O and 5 mL water. The aqueous phase was extracted with 5 mL of Et₂O, and the combined organic phases were washed with 5 mL of satd NaCl solution, dried over MgSO₄, filtered, and concentrated to yield 0.303 g of an orange-brown oil. Column chromatography on 15 g of silica gel (elution with 10% EtOAc–hexanes) afforded 0.086 g (77%) of the resorcinol **40** as a white powder, mp 126–129 °C: IR (neat) 3426, 3054, 2987, 1631, 1422 cm^{–1}; ¹H NMR (300 MHz, CDCl₃) δ 6.25 (s, 1H), 4.67 (s, 1H), 4.43 (s, 1H), 2.59 (t, *J*=7.6 Hz, 2H), 2.19 (s, 3H), 2.08 (s, 3H), 1.33–1.57 (m, 4H), 0.93 (t, *J*=7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 152.6, 151.8, 135.5, 114.2, 112.5, 109.3, 31.8, 23.5, 23.1, 20.3, 14.3, 11.6; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₂H₁₈O₂, 195.1385; found, 195.1386.

4.7.3. 3-Butyl-4-hydroxy-5,6-dimethyl-ortho-quinone (**41**)

A 100-mL, two-necked, round-bottomed flask equipped with a rubber septum and 50-mL addition funnel fitted with an argon inlet adapter was charged with a solution of phenol **26** (0.187 g, 0.533 mmol) in 30 mL of acetone and stirred at rt while a solution of Na₂HPO₄ (0.56 g, 3.9 mmol) and potassium nitrosodisulfonate (0.575 g, 2.1 mmol) in 20 mL of water

was added dropwise over 3 min. The resulting solution was stirred at rt for 24 h and then extracted with three 30-mL portions of EtOAc. The combined organic phases were dried over MgSO₄, filtered, and concentrated to afford 0.163 g of an orange oil. This material was diluted with hexanes and concentrated onto 0.450 g of silica gel, which was transferred to the top of a column of 15 g silica gel. Elution with 0–10% EtOAc–hexanes provided 0.146 g of an orange oil. Further concentration (0.2–0.3 Torr, rt, 1 h) followed by column chromatography on 10 g of silica gel (elution with 5% EtOAc–hexanes) yielded 0.073 g (66%) of quinone **41** as fluorescent orange needles, mp 63–68 °C: IR (KBr) 3392, 2956, 2928, 2859, 1650, 1633, 1620, 1365; ¹H NMR (300 MHz, CDCl₃) δ 6.94 (s, 1H), 2.39–2.46 (m, 2H), 2.04 (t, *J*=1.1 Hz, 3H), 2.03 (t, *J*=1.1 Hz, 3H), 1.26–1.49 (m, 4H), 0.90 (t, *J*=7.1 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 187.6, 184.0, 150.8, 143.8, 136.3, 121.8, 30.7, 23.01, 22.95, 14.1, 13.1, 11.8; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₁₂H₁₆O₃, 209.1172; found, 209.1171.

4.7.4. 5-Triisopropylsiloxy-1,2,3,4,7,8,9,10-octahydrobenzo[d]naphtho[1,2-b]furan (**43**)

A 10-mL round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with a solution of phenol **34** (0.125 g, 0.311 mmol) in 2 mL of CH₂Cl₂ and VO(acac)₂ (0.006 g, 0.02 mmol). The mixture was stirred for 5 min, and then anhydrous TBHP solution (4.0 M in toluene, 0.100 mL, 0.400 mmol) was added. The rubber septum was replaced with a cold finger reflux condenser and the mixture was heated at reflux for 4.5 h. Additional VO(acac)₂ (0.006 g, 0.02 mmol) and TBHP solution (4.0 M in toluene, 0.100 mL, 0.400 mmol) were added, and heating was continued for 2 h. TFA (0.060 mL, 92 mg, 0.81 mmol) was next added and the reaction mixture was heated at reflux for an additional 21 h and then allowed to cool to rt. Concentration afforded 0.260 g of a viscous blue-green oil, which was diluted with CH₂Cl₂ and concentrated onto 0.600 g of silica gel, which was transferred to the top of a column of 20 g of silica gel and eluted with 5% benzene–hexanes to provide 0.068 g (55%) of **43** as a yellow oil: IR (neat) 2940, 1618, 1592, 1507, 1463, 1448 cm^{–1}; ¹H NMR (300 MHz, CDCl₃) δ 6.30 (s, 1H), 2.80–2.87 (m, 4H), 2.74–2.78 (m, 2H), 2.68–2.72 (m, 2H), 1.77–1.92 (m, 8H), 1.34 (sept, *J*=7.8 Hz, 3H), 1.14 (d, *J*=7.5 Hz, 18H); ¹³C NMR (75 MHz, CDCl₃) δ 154.9, 151.9, 148.1, 132.8, 118.2, 114.1, 113.2, 112.2, 30.2, 24.2 (2C), 23.8, 23.54, 23.48, 23.2, 23.1, 18.9, 14.0; HRMS-ESI (*m/z*): [M+H]⁺ calcd for C₂₅H₃₈O₂Si, 399.2714; found, 399.2716.

4.8. Allylation of phenolic benzannulation products

4.8.1. General procedure: 2-propenyl 2-(2-propenyl)-3-triisopropylsiloxy-5,6,7,8-tetrahydronaphthyl ether (**45**)

A 10-mL round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with K₂CO₃ (0.100 g, 0.723 mmol) and NaI (0.021 g, 0.14 mmol) and flame dried under vacuum. The flask was back-filled with argon, allowed

to cool to rt, and a solution of naphthol **35** (0.083 g, 0.23 mol) in 2 mL of acetone was added. Allyl bromide (0.100 mL, 0.140 g, 1.16 mmol) was added, the septum was replaced with a cold finger condenser, and the reaction mixture was heated at reflux for 18 h. Additional allyl bromide (0.100 mL, 0.140 g, 1.16 mmol) was then added, and heating was continued for an additional 18 h. The resulting mixture was allowed to cool to rt and partitioned between 5 mL of Et₂O and 5 mL of water. The aqueous phase was extracted with two 5-mL portions of Et₂O, and the combined organic phases were dried over MgSO₄, filtered, and concentrated to yield 0.171 g of a yellow oil, which was diluted with hexanes and concentrated onto 0.300 g of silica gel, which was transferred to the top of a column of 10 g of silica gel. Elution with 5–10% benzene–hexanes furnished 0.068 g (74%) of allyl ether **45** as a yellow oil: IR (neat) 3078, 2942, 2867, 1637, 1605, 1573, 1477, 1425 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.35 (s, 1H), 6.11 (ddt, $J=17.1$, 10.5, 5.3 Hz, 1H), 6.00 (ddt, $J=17.1$, 10.0, 6.0 Hz, 1H), 5.43 (app dq, $J=17.2$, 1.7 Hz, 1H), 5.24 (app dq, $J=10.5$, 1.5 Hz, 1H), 4.99 (app dq, $J=17.1$, 1.8 Hz, 1H), 4.94 (app dq, $J=10.1$, 1.7 Hz, 1H), 4.38 (dt, $J=5.3$, 1.6 Hz, 2H), 3.41 (dt, $J=6.0$, 1.6 Hz, 2H), 2.64–2.71 (m, 4H), 1.72–1.78 (m, 4H), 1.24–1.36 (m, 3H), 1.11 (d, $J=7.1$ Hz, 18H); ¹³C NMR (75 MHz, CDCl₃) δ 156.3, 152.6, 137.9, 136.4, 134.6, 130.3, 123.1, 121.1, 116.8, 114.4, 73.4, 29.8, 29.2, 23.7, 23.4, 23.3, 18.4, 13.3; HRMS-ESI (m/z): [M+H]⁺ calcd for C₂₅H₄₀O₂Si, 401.2870; found, 401.2861.

4.8.2. 2-Propenyl 2-(3-butenyl)-6-ethyl-5-methyl-3-triisopropylsiloxy-phenyl ether (**44**)

Reaction of phenol **31** (0.083 g, 0.23 mol) with K₂CO₃ (0.100 g, 0.723 mmol), NaI (0.021 g, 0.14 mmol), and allyl bromide (0.200 mL total, 0.280 g, 2.32 mmol) in 2 mL of acetone according to the general procedure and purification by column chromatography on 10 g of silica gel (elution with 0–10% benzene–hexanes) provided 0.060 g (65%) of allyl ether **44** as a yellow oil: IR (neat) 3077, 2945, 2867, 1640, 1603, 1569, 1479 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.41 (s, 1H), 6.11 (ddt, $J=17.2$, 10.4, 5.2 Hz, 1H), 5.91 (ddt, $J=17.1$, 10.2, 6.6 Hz, 1H), 5.46 (app dq, $J=17.1$, 1.7 Hz, 1H), 5.26 (app dq, $J=10.4$, 1.5 Hz, 1H), 5.04 (app dq, $J=17.1$, 1.7 Hz, 1H), 4.96 (dm, $J=10.1$ Hz, 1H), 4.30 (dt, $J=5.2$, 1.6 Hz, 2H), 2.63–2.71 (m, 2H), 2.58 (q, $J=7.5$ Hz, 2H), 2.25–2.34 (m, 2H), 2.23 (s, 3H), 1.22–1.36 (m, 3H), 1.08–1.14 (m, 21H); ¹³C NMR (75 MHz, CDCl₃) δ 156.6, 152.7, 139.4, 134.8, 134.6, 128.5, 123.3, 116.7, 116.4, 114.3, 75.3, 34.4, 24.9, 20.1, 19.6, 18.4, 15.0, 13.4; HRMS-ESI (m/z): [M+H]⁺ calcd for C₂₅H₄₂O₂Si, 403.3027; found, 403.3017.

4.9. Ring closing metathesis

4.9.1. General procedure: 6-triisopropylsiloxy-2,5,8,9,10,11-hexahydronaphtho[1,2-b]oxepine (**47**)

A 50-mL round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with the ruthenium metathesis catalyst **48** (0.006 g, 0.007 mmol), 20 mL of CH₂Cl₂, and a solution of allyl ether **45** (0.056 g, 0.14 mmol) in 10 mL

of CH₂Cl₂. The septum was replaced with a cold finger condenser fitted with an argon inlet and the reaction mixture was heated at reflux for 1 h and then allowed to cool to rt and concentrated to yield 0.080 g of a brown oil. Column chromatography on 5 g of silica gel (elution with 1% EtOAc–hexanes) afforded 0.050 g (96%) of **47** as a yellow oil: IR (neat) 2944, 2867, 1609, 1572, 1481 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.34 (s, 1H), 5.77–5.88 (m, 1H), 5.40 (dm, $J=11.3$ Hz, 1H), 4.52 (app quint, $J=2.4$ Hz, 2H), 3.51 (dd, $J=5.3$, 2.0 Hz, 2H), 2.62–2.69 (m, 4H), 1.70–1.80 (m, 4H), 1.21–1.34 (m, 3H), 1.11 (d, $J=7.0$ Hz, 18H); ¹³C NMR (75 MHz, CDCl₃) δ 157.3, 150.4, 136.2, 127.7, 126.6, 124.5, 122.4, 114.9, 69.9, 29.8, 23.4, 23.3, 23.2, 23.1, 18.3, 13.3; HRMS-ESI (m/z): [M+H]⁺ calcd for C₂₃H₃₆O₂Si, 373.2557; found, 373.2567.

4.9.2. 10-Ethyl-9-methyl-3-triisopropylsiloxy-5,6-dihydro-2H-benzo[b]oxocine (**46**)

Reaction of allyl ether **44** (0.044 g, 0.11 mmol) with ruthenium catalyst **48** (0.005 g, 0.006 mmol) in 25 mL of CH₂Cl₂ according to the general procedure and purification by column chromatography on 5 g of silica gel (elution with 1% EtOAc–hexanes) afforded 0.039 g (95%) of **46** as a yellow oil: IR (neat) 2944, 2867, 1603, 1569, 1465 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.41 (s, 1H), 5.81 (ddt, $J=11.4$, 6.7, 1.5 Hz, 1H), 5.40 (ddt, $J=11.3$, 4.5, 1.2 Hz, 1H), 4.68 (dd, $J=4.6$, 1.3 Hz, 2H), 2.97 (d, $J=6.3$ Hz, 1H), 2.94 (d, $J=4.8$ Hz, 1H), 2.60–2.69 (m, 2H), 2.59 (q, $J=7.5$ Hz, 2H), 2.23 (s, 3H), 1.21–1.35 (m, 3H), 1.11 (d, $J=7.0$ Hz, 18H), 1.12 (t, $J=7.2$ Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 155.8, 152.0, 134.7, 133.5, 128.2, 125.3, 122.4, 116.0, 71.9, 28.0, 25.7, 19.9, 19.6, 18.4, 14.9, 13.3; HRMS-ESI (m/z): [M+H]⁺ calcd for C₂₃H₃₈O₂Si, 375.2714; found, 375.2713.

Acknowledgements

We thank the National Institutes of Health (GM 28273), Merck Research Laboratories, and Boehringer Ingelheim Pharmaceuticals for generous financial support. Y.Z. was supported by a Po Ting Ip Postdoctoral Fellowship and W.F.A. was supported in part by a fellowship from the Kenneth M. Gordon Fund.

References and notes

1. Preliminary communication: Austin, W. F.; Zhang, Y.; Danheiser, R. L. *Org. Lett.* **2005**, *7*, 3905.
2. Reviewed in: (a) Danheiser, R. L.; Dudley, G. B.; Austin, W. F. *Science of Synthesis*; Danheiser, R. L., Ed.; Thieme: Stuttgart, 2006; Vol. 23, pp 493–568; (b) Tidwell, T. T. *Ketenes*, 2nd ed.; John Wiley and Sons: Hoboken, NJ, 2006.
3. (a) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943; (b) Danheiser, R. L.; Gee, S. K.; Sard, H. *J. Am. Chem. Soc.* **1982**, *104*, 7670; (c) Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1672; (d) Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990**, *112*, 3093.
4. For applications in the total synthesis of natural products, see: Dudley, G. B.; Takaki, K. S.; Cha, D. D.; Danheiser, R. L. *Org. Lett.* **2000**, *2*, 3407 and references cited therein.

5. For reviews of the chemistry of silylketenes, see: (a) George, D. M.; Danheiser, R. L. *Science of Synthesis*; Danheiser, R. L., Ed.; Thieme: Stuttgart, Germany, 2006; Vol. 23, pp 53–99; (b) Pons, J.-M.; Kocienski, P. J. *Science of Synthesis*; Fleming, I., Ed.; Thieme: Stuttgart, Germany, 2001; Vol. 4, pp 657–668.
6. (a) Danheiser, R. L.; Sard, H. *J. Org. Chem.* **1980**, *45*, 4810; (b) Loebach, J. L.; Bennett, D. M.; Danheiser, R. L. *J. Org. Chem.* **1998**, *63*, 8380; (c) Bennett, D. M.; Okamoto, I.; Danheiser, R. L. *Org. Lett.* **1999**, *1*, 641.
7. (a) Loebach, J. L.; Bennett, D. M.; Danheiser, R. L. *J. Am. Chem. Soc.* **1998**, *120*, 9690; (b) Dalton, A. M.; Zhang, Y.; Davie, C. P.; Danheiser, R. L. *Org. Lett.* **2002**, *4*, 2465; (c) Rigby, J. H.; Wang, Z. *Org. Lett.* **2003**, *5*, 263; (d) Davie, C. P.; Danheiser, R. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 5867; (e) Moser, W. H.; Feltes, L. A.; Sun, L.; Giese, M. W.; Farrell, R. W. *J. Org. Chem.* **2006**, *71*, 6542.
8. For related reactions involving silylated bisketenes, see: (a) Colomvakos, J. D.; Egle, I.; Ma, J.; Pole, D. L.; Tidwell, T. T.; Warkentin, J. J. *Org. Chem.* **1996**, *61*, 9522; (b) Huang, W.; Tidwell, T. T. *Synthesis* **2000**, 457; (c) Allen, A. D.; Huang, W.-W.; Moore, P. A.; Far, A. R.; Tidwell, T. T. *J. Org. Chem.* **2000**, *65*, 5676.
9. (a) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959; (b) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G. *Organic Syntheses*; Wiley: New York, NY, 1998; Collect. Vol. IX, p 197.
10. (a) Maas, G.; Brückmann, R. *J. Org. Chem.* **1985**, *50*, 2801; (b) Brückmann, R.; Schneider, K.; Maas, G. *Tetrahedron* **1989**, *45*, 5517.
11. For reviews of the chemistry of ynoates, see: (a) Shindo, M. *Tetrahedron* **2007**, *63*, 10; (b) Shindo, M. *Synthesis* **2003**, 2275; (c) Shindo, M. *Chem. Soc. Rev.* **1998**, *27*, 367.
12. Kowalski, C. J.; Lal, G. S.; Haque, M. S. *J. Am. Chem. Soc.* **1986**, *108*, 7127.
13. Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4464.
14. (a) Julia, M.; Saint-Jalmes, V. P.; Verpeaux, J.-N. *Synlett* **1993**, 233; (b) Julia, M.; Saint-Jalmes, V. P.; Plé, K.; Verpeaux, J.-N.; Hollingworth, G. *Bull. Soc. Chim. Fr.* **1996**, *133*, 15.
15. For a discussion of the 6π electrocyclicization of 3-oxido-1,3,5-hexatrienes, see: Magnus, P. *Nouv. J. Chim.* **1978**, *2*, 555.
16. For prior examples of 6π electrocyclicization reactions involving enolate derivatives, see: (a) White, J. D.; Skeeane, R. W. *J. Am. Chem. Soc.* **1978**, *100*, 6296; (b) White, J. D.; Skeeane, R. W.; Trammell, G. L. *J. Org. Chem.* **1985**, *50*, 1939; (c) Magomedov, N. A.; Ruggiero, P. L.; Tang, Y. *J. Am. Chem. Soc.* **2004**, *126*, 1624; (d) Magomedov, N. A.; Ruggiero, P. L.; Tang, Y. *Org. Lett.* **2004**, *6*, 3373 and references cited therein.
17. For a recent theoretical study and leading references, see: Takahashi, M.; Kira, M. *J. Am. Chem. Soc.* **1999**, *121*, 8597.
18. (a) Moser, W. H.; Sun, L.; Huffman, J. C. *Org. Lett.* **2001**, *3*, 3389; (b) Fogel, L.; Hsung, R. P.; Wulff, W. D.; Sommer, R. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **2001**, *123*, 5580; (c) Chamberlin, S.; Wulff, W. D. *J. Org. Chem.* **1994**, *59*, 3047.
19. Blanco, S. E.; Almandoz, M. C.; Ferretti, F. H. *Spectrochim. Acta, Part A* **2005**, *61*, 93 and references cited therein.
20. Yu, W.; Jin, Z. *Tetrahedron Lett.* **2001**, *42*, 369.
21. The metalation of 1-phenyl-4-penten-1-yne with MeLi has previously been reported: Klein, J.; Brenner, S.; Medlik, A. *Isr. J. Chem.* **1971**, *9*, 177.
22. Separation of these phenols from byproducts was not possible without significant losses, precluding an accurate determination of yield.
23. A related thermal 1,3 carbon to oxygen shift in a 2-*tert*-butyldimethylsilyl-substituted phenol has recently been reported: Eastham, S. A.; Ingham, S. P.; Hallett, M. R.; Herbert, J.; Quayle, P.; Raftery, J. *Tetrahedron Lett.* **2006**, *47*, 2299.
24. Thermal 1,3-rearrangement of 2-trimethylsilylphenol has previously been described: Cooper, G. D. *J. Am. Chem. Soc.* **1961**, *26*, 925.
25. For a review of palladium-catalyzed cyclizations of this type, see: Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285.
26. These conditions have been employed by Hegedus for the cyclization of 2-allylanilines to indoles, see: Hegedus, L. S.; Allen, G. F.; Bozell, J. J.; Waterman, E. L. *J. Am. Chem. Soc.* **1978**, *100*, 5800.
27. Lattanzi, A.; Senatore, A.; Massa, A.; Scettri, A. *J. Org. Chem.* **2003**, *68*, 3691.
28. For reviews of the application of ring closing metathesis to the preparation of heterocycles, see: (a) Chattopadhyay, S. K.; Karmakar, S.; Biswas, T.; Majumdar, K. C.; Rahaman, H.; Roy, B. *Tetrahedron* **2007**, *63*, 3919; (b) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199.
29. Hill, J. G.; Rossiter, B. E.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3607.
30. (a) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165; (b) Ellison, R. A.; Griffin, R.; Kotsonis, F. N. *J. Organomet. Chem.* **1972**, *36*, 209.
31. Danheiser, R. L.; Helgason, A. L. *J. Am. Chem. Soc.* **1994**, *116*, 9471.
32. Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 10204.
33. Sweis, R. F.; Schramm, M. P.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 7442.
34. Sun, J.; Kozmin, S. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4991.
35. LiHMDS solution was prepared by the reaction of HMDS (2.8 mL, 2.1 g, 13 mmol) with 5.0 mL of BuLi solution (2.49 M in hexanes, 13 mmol) in 6.4 mL of THF.
36. Akai, S.; Kitagaki, S.; Naka, T.; Yamamoto, K.; Tsuzuki, Y.; Matsumoto, K.; Kita, Y. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1705.