Compounds 1-OPO(OMe)$_2$ and 1-OPS(OMe)$_2$ (7 mg) were mixed separately with 0.6 mL of stock solution (40 mM). Spectra were recorded at 20 ± 1 °C. A solution of 2-SPO(OMe)$_2$ (60 mM) was divided into 500-μL portions and frozen at −20 °C. The samples were allowed to thaw in a water bath at the appropriate temperature and to equilibrate in the probe for 5 min before spectra were recorded. A 90 mM solution of 1-SPO(OMe)$_2$ was divided into glass ampules and flame-sealed. Samples were heated in an oil bath, removed periodically, placed in an ice water bath to quench the reaction, and stored at 4 °C until analysis. Upon completion of a kinetic run, ^{31}P NMR spectra were recorded.

Reactions were monitored for at least 2 half-lives. Each kinetic point was the average of 10 aquisitions during a period of 20 s with a delay of at least 6 T_1's between radio frequency pulses. Measurements of the points from sealed ampules used 100 acquisitions with a similar delay. ^{31}P NMR signals were referenced to trimethyl phosphate in benzene contained in a coaxial tube.

Product Studies. NMR samples for each phosphorothioate were diluted with an equal volume of diethyl ether and water and mixed. The ether phase was dried, and solvent was removed by rotary evaporation. The residue was passed through a short bed of silica prior to GC analysis. Peaks for the products were identified by coinjection with known compounds. The volume of the aqueous phase was reduced by lyophilization, and components were analyzed by ^{31}P NMR with addition of known samples to confirm peak assignments. Intensities of ^{31}P NMR signals were compared to external solutions of trimethyl phosphate in benzene or 1 M phosphoric acid in D_2O in a coaxial tube. Material balances of water-soluble (phosphorothioates) and extractable (alcohols and TFE ethers) compounds were greater than 85%.

Solvolysis of Geranyl Tosylate (1-OTs) in 65:35 TFE/D_2O Containing 5. KH (0.12 g, 3.0 mmol) was rinsed twice with 4 mL of diethyl ether, and excess ether was removed by a gentle stream of nitrogen. THF (2 mL) was added, and 0.46 g (3.0 mmol) of geraniol was added in 1 mL of THF. The solution was stirred at room temperature for 0.5 h and then cooled to −78 °C in an acetone/dry ice bath. Tosyl chloride (0.57 g, 3.0 mmol) was added, and the solution was allowed to stir for 0.5 h. The volume of the solution was reduced to approximately 1 mL under high vacuum. The flask was removed from the bath, and 4 mL of a solution containing 65:35 (v/v) TFE/D_2O, 0.4 M 2,6-lutidine, and 1 mmol of **5** (lutidinium form) at 20 °C was added. The mixture was shaken vigorously for 1 min. Pentane/diethyl ether (1:1) and water were added. The layers were separated, and pentane/ether was removed by rotary evaporation to give 0.43 g of a mixture of phosphorothioates, alcohols, and TFE ethers. The residue was analyzed by ^{31}P NMR; peaks were seen at δ 69.5, 29.4, and 25.4 with respective relative intensities of 1, 50, and 5 for 1-OPS(OMe)$_2$, 1-SPO(OMe)$_2$, and 2-SPO(OMe)$_2$.

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Palladium-Catalyzed Oxyhexatriene Cyclization: A Novel Approach to Cyclohexenone Annulation[1]

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Abstract: Palladium(II) catalysts mediate the cyclization of [(trimethylsilyl)oxy]hexatrienes (SOHs) to afford cyclohexenones. This novel reaction represents the first general approach to the hexatriene cyclization of dienone enolates or their derivatives. Fully-conjugated dienones are readily converted to the kinetic enolates with LDA and trapped as the silyl enol ethers. Heating of these compounds in refluxing toluene or xylenes in the presence of 5 mol % Pd(PFu$_3$)$_2$Cl$_2$ gives the corresponding cyclohexenones in good yield. Substituents α to the carbonyl interfere with the cyclization. Treatment of cross-conjugated dienones with LDA causes formation of the *trans*-SOH. However, cis/trans isomerization occurs under the reaction conditions, and cyclization still proceeds, albeit in moderate yields. Attempts at thermal cyclization of the kinetic potassium or lithium enolates of 1-acetyl-2-vinylcyclohex-2-ene or the corresponding SOH in the absence of a palladium catalyst led to little or no cyclohexenone formation. This observation confirms that the cyclization is catalyzed by palladium and suggests that the concerted thermal electrocyclization of electron-rich hexatrienes may be a difficult process. Pd(PFu$_3$)$_2$Cl$_2$ is proposed to mediate SOH cyclization by causing palladium enolate formation, followed by addition across a distal carbon–carbon double bond and trapping of the annulated product as the silyl enol ether.

The synthesis of six-membered rings has traditionally been one of the most important endeavors of the synthetic organic chemist, leading to a number of methods for the formation of cyclohexenones.[2,3] The most utilized approach, the Robinson annulation, involves the Michael addition of an enolate to an alkyl vinyl ketone followed by aldol condensation of the resulting 1,4-dione (Scheme I).[3] Many modifications of the Michael/aldol scheme have been made, all of which lead to compounds of comparable regiochemistry.[3] Martin[4] and Fuchs[5] have developed conjugate addition/intramolecular Wittig approaches to cyclohexenone annulation that allow somewhat greater variation in the products available.

While studying a route for the total synthesis of corticosteroids, we required a facile conversion of a cyclohexanone into the corresponding Δ^2-bicyclo[4.4.0]decen-2-one. Unfortunately, none of the aforementioned methodology appeared suitable for our needs. In 1978 Magnus proposed a general approach to the annulation of cyclohexenones involving the thermal cyclization of enolates derived from acyclic dienones.[6] To date, this proposal, based on earlier findings of Scanio[7] and Yoshikoshi,[8] has not been tested. We observed that the thermal (110 °C) cyclization of a hexatrienolate proceeds very slowly to afford cyclohexenones in low yield.

Herein, we report the first general cyclization of hexatrienolate derivatives. Palladium complexes mediate the cyclization of [(trimethylsilyl)oxy]hexatrienes (SOHs) to afford cyclohexenones after deprotection. As shown in Scheme I, the SOH cyclization is complementary to both the Robinson and the Martin–Fuchs

(1) (a) Presented in part at the 197th National Meeting of the American Chemical Society, 9–14 April 1989, Dallas, TX; ORGN 151. (b) Presented in part at the Fifth IUPAC Symposium on Organometallic Chemistry Directed Towards Organic Synthesis; 1–6 Oct 1989, Florence, Italy; Abstract No. OP-B33.

(2) Jung, M. E. *Tetrahedron* **1976**, *32*, 3–31.

(3) Gawley, R. E. *Synthesis* **1976**, 777–794.

(4) (a) Martin, S. F.; Desai, S. R. *J. Org. Chem.* **1977**, *42*, 1664–1666. (b) Martin, S. F.; Desai, S. R. *J. Org. Chem.* **1978**, *43*, 4673–4675.

(5) Pariza, R. J.; Fuchs, P. L. *J. Org. Chem.* **1983**, *48*, 2304–2306.

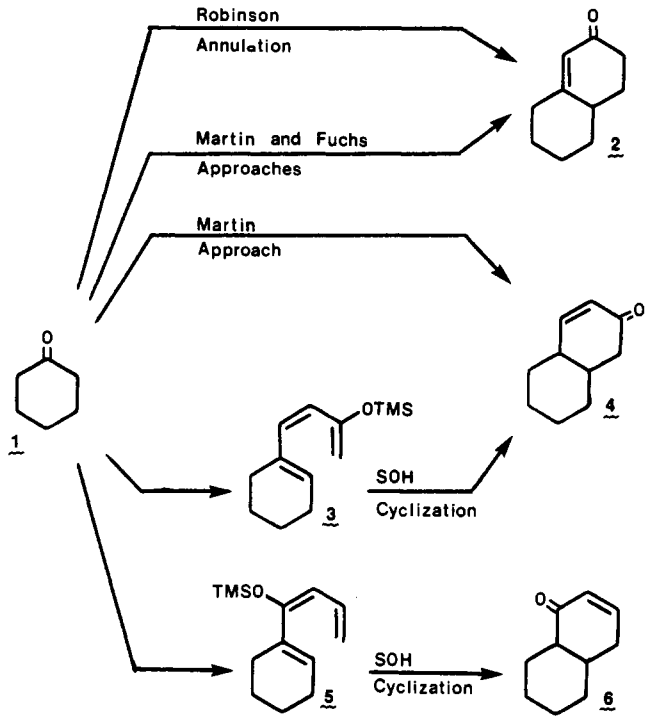
(6) Magnus, P. *Nouv. J. Chim.* **1978**, *2*, 555–557.

(7) Scanio, C. J. V.; Starrett, R. M. *J. Am. Chem. Soc.* **1971**, *93*, 1539–1540.

(8) Miyashita, M.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1974**, *96*, 1917–1925.

0002-7863/91/1513-4903$02.50/0

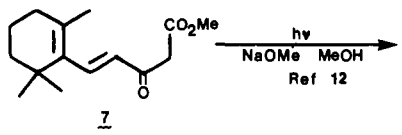
Scheme I



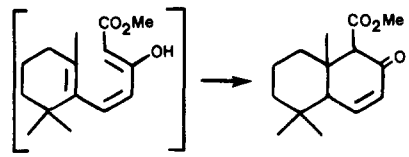
annulations. The Robinson annulation and its modifications,[2,3] as well as the Martin–Fuchs approaches,[4,5] lead to the formation of $\Delta^{1(10)}$-bicyclo[4.4.0]decen-2-one (**2**) (Scheme I). In contrast, cyclization of [(trimethylsilyl)oxy]hexatriene **3**, readily formed from the corresponding fully-conjugated dienone, gives the Δ^1-en-3-one, **4**, a product also available from a variation of Martin's scheme.[4] Cyclization of SOH **5**, generated retrosynthetically from the cross-conjugated dienone, affords Δ^2-en-1-one **6**, the regioisomer needed for our corticoid synthesis.

Results and Discussion

Thermal Oxyhexatriene Cyclization Approach. Our original approach to the annulation of cyclohexenones involved the thermal electrocyclization of an enolate derived from a dienone. Thermal hexatriene cyclizations have become increasingly useful for the synthesis of six-membered rings,[9,10] but typically the hexatriene of interest contains either electron-withdrawing groups or no heterofunctionality.[11] We have been studying the ability of electron-rich hexatrienes to undergo similar electrocyclic rearrangements. Scanio and Starrett proposed that a hexatrienolate intermediate is involved in product formation when the Robinson annulation is performed in DMSO.[7] Yoshikoshi also invoked such an intermediate to explain the formation of a bicyclodecenone on treatment of a cyclodeca-2,8-dien-1-one with a Wittig reagent in DMSO.[8] In both cases, the products were formed at room temperature over a few hours. While studying a related annulation, White found that *trans*-enol **7** underwent photochemical trans/cis isomerization, followed by enolate formation and photochemical isomerization to afford bicyclic products.[12] Photochemical hexatrienolate cyclization was made possible in this case by extending the conjugate of the hexatrienolate system with an ester group.

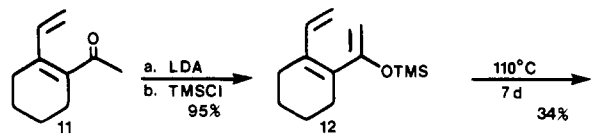


7

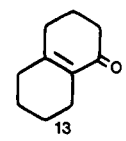


We chose the kinetic enolate of 1-acetyl-2-vinylcyclohexene (**11**) as a model for the hexatrienolate cyclization in order to optimally set the hexatriene framework for cyclization. Dienone **11** was readily available by formation of the thermodynamic mesylate of 2-acetyl-1-cyclohexanone (70% yield), followed by Pd-$(PPh_3)_4$-catalyzed coupling of the mesylate with vinyltrimethyltin in the presence of a stoichiometric amount of LiBr (74%).[13] Treatment of dienone **11** with either LDA or potassium hexamethyldisilazide in THF resulted in clean formation of the desired enolate, as shown by trapping in situ with trimethylsilyl chloride. No products of cyclization were observed, even after extended reaction times. Similarly, the reaction of **11** with KH in DMSO produced the desired enolate, but only traces of annulated materials were detected even after extended reaction times. These results suggest that the cyclizations reported by Scanio and Yoshikoshi may be occurring through more complex mechanisms than were originally assumed.[7,8] Attempts at photochemical cyclization of hexatrienolates or the corresponding silyl enol ethers proved equally disappointing.

Theoretical studies have indicated that electron-donating groups will act to disfavor a concerted thermal hexatriene cyclization.[14] As a test, silyl enol ether **12** was heated in toluene at 110 °C for 48 h during which no annulation was observed. Continued heating over a total of 7 days afforded $\Delta^{5,10}$-bicyclo[4.4.0]decen-1-one (**13**) and 5,6,7,8-tetrahydro-1-naphthol (**14**) in a 1:1 ratio. The long reaction times required for the electrocyclic reaction indicated to us that optimization of the oxyhexatriene cyclization might require some method to remove electron density from the hexatrienol system while retaining the oxygen substituent.



11 **12**



13

Metal-Catalyzed Oxyhexatriene Cyclization. Transition metals have been used extensively to mediate cyclizations and coupling reactions of unsaturated systems.[15,16] We therefore chose to

(9) For a discussion of the hexatriene cyclization, see: Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Deerfield Beach, FL, 1970; pp 51–53.

(10) For some recent applications of six-membered ring annulation using nonanionic hexatriene cyclizations, see: (a) Nicolaou, K. C.; Zipkin, R. E.; Uenishi, J. *J. Am. Chem. Soc.* **1982**, *104*, 5555-5557. (b) Reischel, W.; Okamura, W. *J. Am. Chem. Soc.* **1982**, *104*, 6115–6117. (c) Gilchrist, T. L.; Summersell, R. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2595–2601. (d) Gilchrist, T. L.; Summersell, R. J. *J. Chem. Soc., Perkin Trans. 1*, **1988**, 2603–2606.

(11) (a) Marvell, E. N. *Thermal Electrocyclic Reactions*; Academic Press: New York, 1980; pp 260–375. (b) Epiotis, N. D. *J. Am. Chem. Soc.* **1973**, *95*, 1200–1206. (c) Spangler, C. W.; Jondahl, T. P.; Spangler, B. *J. Org. Chem.* **1973**, *38*, 2478–2484.

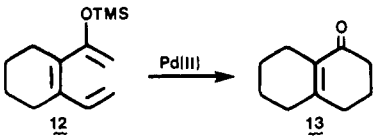
(12) White, J. D.; Skeean, R. W. *J. Am. Chem. Soc.* **1978**, *100*, 6292–6297.

(13) Hettrick, C. M.; Kling, J. K.; Scott, W. J. *J. Org. Chem.* **1991**, *56*, 1489–1492.

(14) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877–1884.

(15) For general monographs of organo-transition-metal chemistry, see: (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications or Organotransition Metal Chemistry*, 2nd ed.; University Science Books: Mill Valley, CA, 1987. (b) Yamamoto, A. *Organotransition Metal Chemistry*; Wiley: New York, 1986. (c) Colquhoun, H. M.; Holton, J.; Thompson, D. J.; Twigg, M. V. *New Pathways for Organic Synthesis: Practical Applications of Transition Metals*; Plenum Press: New York, 1984. (d) Heck, R. F. *Palladium Reagents in Organic Synthesis*: Academic Press: New York, 1985.

Table I. Effect of Selected Palladium Catalysts in the Cyclization of **12**



catalyst	bath temp, °C	reactn time, h	isolated yield of **13**,[a] %
no catalyst	110	48	0
no catalyst	110	168	34
$Pd(OAc)_2/2PPh_3$	110	48	0
$(dppf)PdCl_2$	110	48	(35)[b]
$Pd(PPh_3)_2Cl_2$	110	48	41
$Pd(PPh_3)_4$	110	48	0
$Pd(PFu_3)_2Cl_2$ (**15**)	115	72	84

[a] Yield based on GC analysis. [b] Reaction with $(dppf)PdCl_2$ led to a complex mixture of products.

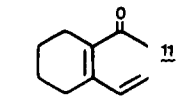
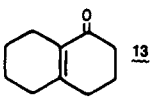
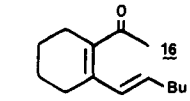
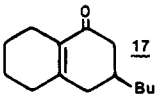
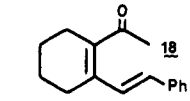
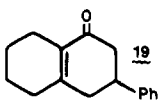
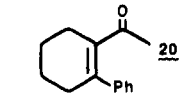
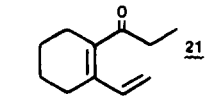
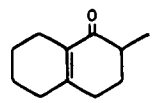
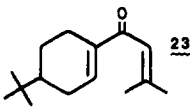
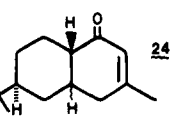
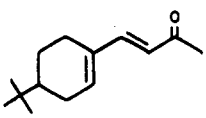
investigate a similar approach for the annulation of the [(trimethylsilyl)oxy]hexatriene (SOH) system. During a preliminary survey of possible catalysts, it was found that Wilkinson's catalyst ($Rh(PPh_3)_3Cl$) is very inefficient at effecting the cyclization. Treatment of SOH **12** with 5 mol % Wilkinson's catalyst in toluene at 110 °C for 72 h afforded none of the desired enone. Reaction with the catalyst in benzene at 65 °C for 120 h afforded cyclized enone **13** in only 12% yield. The major product of these reactions was deprotected dienone **11**, isolated in 55% yield. In contrast, use of the isoelectronic $Ru(PPh_3)_3Cl_2$ afforded enone **13** in 63% yield as a part of a complex mixture of products that included dienone **11** and phenol **14**.

Treatment of SOH **12** with Pd(II) catalysts in refluxing toluene or xylenes afforded cyclized enone **13** in variable yields along with deprotected starting material and, in some cases, products of side reactions. As shown in Table I, $Pd(OAc)_2/2PPh_3$ afforded no cyclized material, while $Pd(PPh_3)_2Cl_2$ gave enone **13** in moderate yields. As mentioned above, little cyclization was observed in the absence of a catalyst.

Because palladium catalysts appeared to cause the fewest side reactions, it was decided to optimize the palladium-mediated SOH cyclization. Operating on the hypothesis that electron-poor palladium complexes might favor enone formation, a new Pd(II) complex was synthesized using the relatively electron-poor tri-2-furylphosphine[17] (PFu_3) as the stabilizing ligand. Treatment of K_2PdCl_4 with 2 equiv of PFu_3 in aqueous acetone afforded $Pd(PFu_3)_2Cl_2$ (**15**) in 35% yield as a microcrystalline yellow solid. Analysis of a slurry of the complex in sulfolane by fast atom bombardment mass spectrometry (FAB-MS) scanning between m/z 300 and 800 as described previously[18] afforded no ions that could be assigned to palladium-containing species. In contrast, analysis of a saturated solution of **15** in CH_2Cl_2 using sulfolane as the matrix solvent produced ions at m/z 604 ($Pd(PFu_3)_2Cl_2$ - HCl), 570 (47, $Pd(PFu_3)_2Cl_2$ - 2 Cl), 503 (35, $Pd(PFu_3)_2Cl_2$ - 2 Cl - C_4H_3O), and 338 (68, $Pd(PFu_3)_2Cl_2$ - 2 Cl - PFu_3). The relative intensities of the isotope pattern centered around m/z 604 (relative intensity 95%) matched the calculated intensities for an ion with formula $C_{24}H_{17}ClO_6P_2Pd$.

NMR spectra of microcrystalline **15** in $CDCl_3$ indicated the presence of two isomers in a 1.8:1.0 ratio. Stereochemistry was

Table II. $Pd(PFu_3)_2Cl_2$-Catalyzed Cyclization of Dienones via the Silyl Enol Ethers (SOHs)

entry	dienone	cyclized product	isolated yield, %
1	 **11**	 **13**	84
2	 **16** Bu	 **17** Bu	83
3	 **18** Ph	 **19** Ph	80
4	 **20** Ph	—	0
5	 **21**	 **22**	4
6	 **23**	 **24**	34 (2:1 cis:trans)
7	 **25**	—	0

assigned according to the general observation that the ^{31}P chemical shifts for *cis*-dichlorobis(phosphine)palladium(II) complexes appear downfield from those of the trans isomers.[19] The cis isomer (62%) displayed a singlet in the ^{31}P NMR spectrum at δ -22.3 and ^1H NMR absorbances at δ 6.53, 7.18, and 7.46.[20] The trans isomer (38%) was observed as a singlet in the ^{31}P NMR spectrum at δ -29.1, with ^1H NMR resonances at δ 6.42, 7.31, and 7.54. After the mixture was allowed to stand in $CDCl_3$, tri-2-furylphosphine oxide was slowly formed, presumably by air oxidation of complex **15**.[22] Recrystallization of **15** from hexane/CH_2Cl_2 gave a crystal of $Pd(PFu_3)_2Cl_2$ of marginal quality, which clearly indicated cis stereochemistry of the ligands about the square-planar palladium.[24,25]

(16) For reports on palladium catalysis of electrocyclic reactions, see: (a) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579–586, and references therein. (b) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205–247, and references therein. (c) van der Baan, J. L.; Bickelhaupt, F. *Tetrahedron Lett.* **1986**, *27*, 6267–6270.

(17) For reports on the use of tri-2-furylphosphine as a stabilizing ligand in palladium-catalyzed coupling reactions, see: (a) Farina, V.; Baker, S. R.; Benigni, D. A.; Sapino, C., Jr. *Tetrahedron Lett.* **1988**, *29*, 5739–5742. (b) Farina, V.; Baker, S. R.; Sapino, C., Jr. *Tetrahedron Lett.* **1988**, *29*, 6043–6046.

(18) Mallis, L. M.; Scott, W. J. *Org. Mass Spectrom.* **1990**, *25*, 415–419.

(19) (a) Grim, S. O.; Keiter, R. L. *Inorg. Chim. Acta* **1970**, *4*, 56–60. (b) Mann, B. E.; Masters, B. L.; Shaw, B. L.; Slade, R. M.; Stainback, R. E. *Inorg. Nucl. Chem. Lett.* **1971**, *7*, 881–885. (c) Verstuyft, A. W.; Nelson, J. H.; Cary, L. W. *Inorg. Nucl. Chem. Lett.* **1976**, *12*, 53–58. (d) Verstuyft, A. W.; Redfield, D. A.; Cary, L. W.; Nelson, J. H. *Inorg. Chem.* **1977**, *16*, 2776–2786. (e) MacDougal, J. J.; Nelson, J. H. *Inorg. Nucl. Chem. Lett.* **1979**, *15*, 315–316.

(20) Characteristics of tri-2-furylphosphine: mp 58–60 °C (lit.[21a] mp 63 °C); bp (bulb-to-bulb) 130–140 °C (0.05 mmHg) [lit.[21a] bp 136 °C (4 mmHg)]; IR ($CDCl_3$) 3100, 1535, 1440, 1350, 1195, 1135, 1100, 985 cm^{-1}; ^1H NMR (300 MHz) δ 6.40 (m, 1 H), 6.79 (m, 1 H), 7.65 (br s, 1 H); $^{13}C\{^1H\}$ NMR (75 MHz) δ 110.7 (d, J_{P-C} = 7.0 Hz), 121.1 (d, J_{P-C} = 25.5 Hz), 147.5 (d, J_{P-C} = 3.0 Hz), 148.8 (d, J_{P-C} = 3.7 Hz); $^{31}P\{^1H\}$ NMR (121.5 MHz) δ -77.2 (s).

(21) (a) Niwa, E.; Aoki, H.; Tanaka, H.; Munakata, K. *Chem. Ber.* **1966**, *99*, 712–714. (b) Taddei, F.; Vivarelli, P. *Org. Mag. Reson.* **1970**, *2*, 319–321.

(22) Characteristics of tri-2-furylphosphine oxide: mp 111–112 °C (lit.[23] mp 113–114 °C); bp (bulb-to-bulb) 170–180 °C (0.1 mmHg); IR ($CDCl_3$) 1550, 1450, 1365, 1215, 1130, 1000 cm^{-1}; ^1H NMR (300 MHz) δ 6.53 (m, 1 H), 7.14 (m, 1 H), 7.71 (m, 1 H); $^{13}C\{^1H\}$ NMR (75 MHz) δ 111.0 (d, J_{P-C} = 9.3 Hz), 123.4 (d, J_{P-C} = 22.1 Hz), 148.7 (d, J_{P-C} = 8.6 Hz), 149.0 (d, J_{P-C} = 41.5 Hz); $^{31}P\{^1H\}$ NMR (121.5 MHz) δ -11.7 (s).

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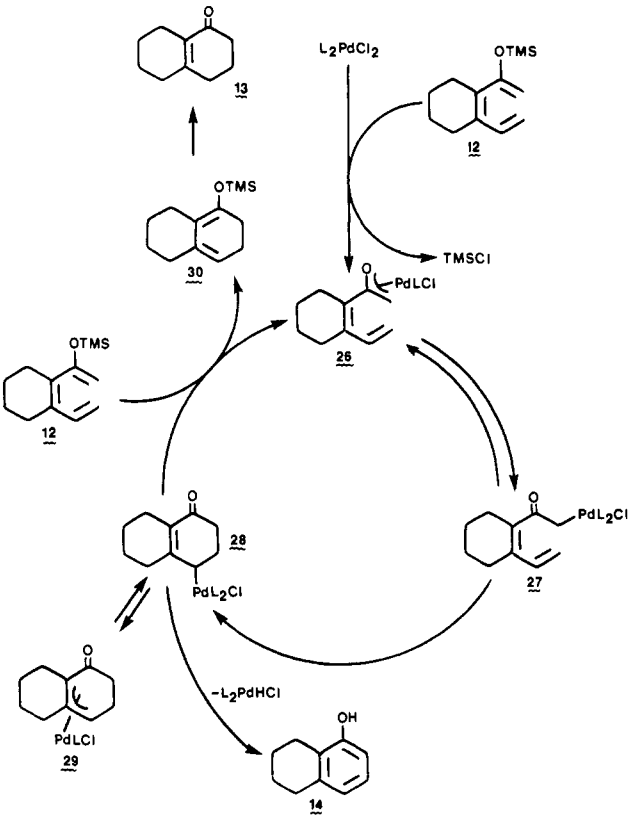
Heating of a toluene or xylenes solution of SOH **12** at the reflux temperature in the presence of substoichiometric amounts of catalyst **15** afforded annulated cyclohexenone **13** in 70–85% yield, along with small amounts of deprotected starting material **11** (Table I). As shown in Table II, analogues of fully-conjugated dienone **11** with substituents on the distal olefin undergo the two-step annulation in consistently high yield (entries 2 and 3). In these cases the cyclization is very clean, affording the annulated product occasionally contaminated with minor amounts of deprotected starting material. Interestingly, the presence of a phenyl group in dienone **18** did not appear to alter the course of the reaction. Analogues of dienone **11** with substituents α to the carbonyl give very little cyclized material (entry 5). The one example to date of the annulation of a cross-conjugated dienone afforded cyclized products in moderate yield (entry 6).

The SOH cyclization may be viewed as being mechanistically similar to an intramolecular Heck olefination.[26-30] The intramolecular Heck olefination involves the palladium-mediated cyclization of a molecule containing both an electrophilic site and a distal olefin. The electrophile may contain one of a wide variety of leaving groups but must contain an sp^2 or sp center at or adjacent to the leaving group. A Pd(0) catalyst (either added or formed in situ) is allowed to undergo oxidative addition with an electrophile to form an organopalladium(II) complex.[31] Insertion across a remote carbon–carbon double bond causes ring formation with generation of a new palladium–carbon σ bond. β-Hydride elimination affords the corresponding olefin with concomitant formation of a palladium(II) hydride. Finally, reaction with base regenerates the Pd(0) catalyst. Recently, a rich chemistry of palladium-catalyzed cyclization of polyene species affording polycyclic compounds has been developed by Overman,[32] Negishi,[33] and Grigg.[34]

Scheme II



The SOH cyclization may be rationalized as involving the transmetallation of the O-Si bond of **12** to form an (oxyallyl)palladium species and TMSCl (Scheme II).[35] This is reminiscent of the first step of the Saegusa oxidation.[36,37] At the reaction temperature, TMSCl is driven from solution. Equilibration to σ-allyl complex **27** followed by addition across the terminal double

(25) The tendency of $Pd(PFu_3)_2Cl_2$ to have cis stereochemistry may be contrasted with $Pd(PPh_3)_2Cl_2$, which exists in solution as a 1:15.5 cis to trans mixture[19e] and has not been crystallized with cis stereochemistry despite repeated attempts. (a) Clark, D. T.; Dillon, K. B.; Thomas, H. R.; Waddington, T. C. *J. Chem. Soc., Dalton Trans.* **1979**, 250–253. (b) Ferguson, G.; McCrindle, R.; McAlees, A. J.; Parvez, M. *Acta Crystallogr., Sect. B* **1982**, *B38*, 2679–2681.

(26) Heck, R. F. *Org. React. (N.Y.)* **1982**, *27*, 345–390.

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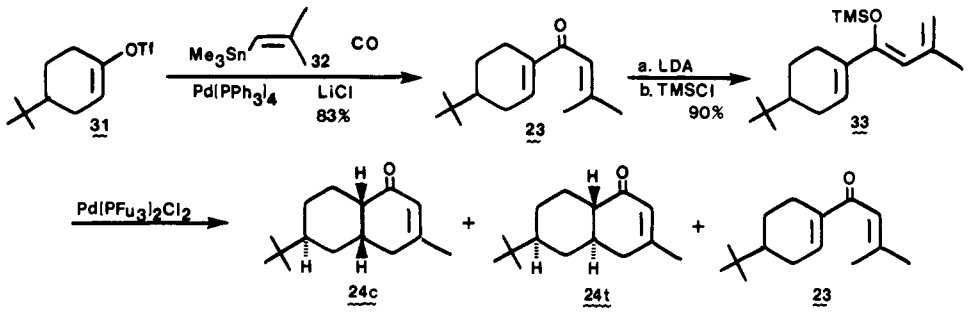
(35) A reviewer has proposed an alternate mechanism involving a one-electron transfer from the silyl enol ether to the Pd(II) catalyst, cyclization of the electron-poor radical cation of the hexatriene, and one-electron transfer from the radical anion of the Pd(II) catalyst to the cyclized radical cation. This interesting proposal, while not disproven, fails to explain the formation of isomerized silyl enol ether **43** and fails to explain why SOH **33** will undergo cyclization but the SOH derived from dienone **25** will not cyclize.

Scheme III. Cross-Conjugated Annulation

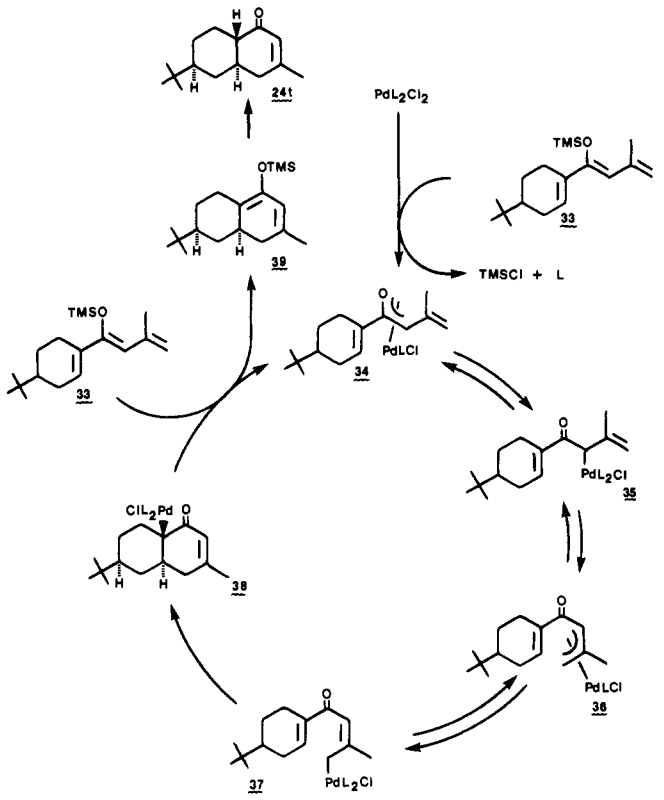


bond[37,38] then affords σ-allylpalladium species **28**. Although complex **28** may be in equilibrium with a number of σ- and π-isomers, trapping of any of these palladium enolates by reformation of the O–Si bond generates the silyl enol ether **30**. Because the reaction is run well above the boiling point of TMSCl, the source of the silyl trapping group must be unreacted silyl ether **12**. Bergman and Heathcock have demonstrated that an (oxyallyl)rhodium complex will equilibrate with a silyl enol ether.[39]

The proposed mechanism allows a number of predictions about the limitations of the annulation. First, addition of excess TMSCl to the reaction mixture and running the reaction in a sealed flask was found to severely slow the reaction and to lower the final yield of annulated product. This is consistent with a reversible preliminary step involving palladium enolate formation. Also, σ-allylpalladium species **28** should be capable of undergoing β-hydride elimination, leading eventually to phenol **14**. Indeed, **14** has been observed in minor amounts (10–20% yield) from the $Pd(PPh_3)_2Cl_2$-mediated cyclization.

More importantly, the proposed mechanism allows the prediction that the stereochemistry of the SOH system will be relatively unimportant, assuming that the intermediate allyl species can isomerize as necessary prior to insertion into the terminal double bond. To test this prediction, two model compounds were synthesized, only one of which is capable of the required isomerization. For the examination of the propensity toward isomerization followed by cyclization, cross-conjugated dienone **23**, obtained by carbonylative coupling[40] of vinyl triflate **31** with (2-methylprop-1-en-1-yl)trimethyltin, was treated with LDA followed by TMSCl to give SOH **33** (83%) as the only product observed (Scheme III). Heating of **33** in the presence of substoichiometric amounts of $Pd(PFu_3)_2Cl_2$ afforded a 2:1 mixture of readily separated diastereomeric decalenones, identified as cis-fused enone **24c** and trans-fused enone **24t** in 34% isolated yield, along with a 61% yield of **23** (Table II, entry 6). The assignment of the major product as the cis isomer was based largely on the upfield shifts observed in the carbon NMR of **24c**, as compared to that of **24t**. Such shielding is well precedented for the bicyclo[4.4.0]decane system.[41] In addition, the ^{13}C NMR of the less polar compound (**24t**) displayed signals at 126.3, 160.8, and 201.3 ppm, in good agreement with those reported for

Scheme IV. Proposed Mechanism for the Formation of **24t**



trans-3-methylbicyclo[4.4.0]dec-2-en-1-one (126.2, 160.5, 200.8 ppm).[42] The more abundant, more polar compound (**24c**) showed signals at 125.2, 161.7, and 203.6 ppm, which correspond well with those reported for *cis*-3-methylbicyclo[4.4.0]dec-2-en-1-one (125.5, 160.2, 201.6 ppm).[42]

As shown in Scheme IV, formation of the observed products may be rationalized as occurring by transmetallation to give (π-oxyallyl)palladium **34**. Equilibration and bond rotation would cause the formation of σ-allylpalladium complex **35**, which would then further equilibrate to the more stable π-allylpalladium complex **36**. Addition across the ring double bond (illustrated for the formation of the trans-ring juncture) followed by trapping of the palladium enolate affords silyl enol ethers, which are subsequently quenched to give enones **24c** and **24t**. The ratio of **24c** to **24t** is determined by facial differences in the hindrance to initial palladium complexation to the olefin. In this case, there appears to be little differentiation.

The high level of returned starting material appears to be the result of a side reaction. In a separate experiment, silyl enol ether **43** was isolated in addition to the normal mixture of products and

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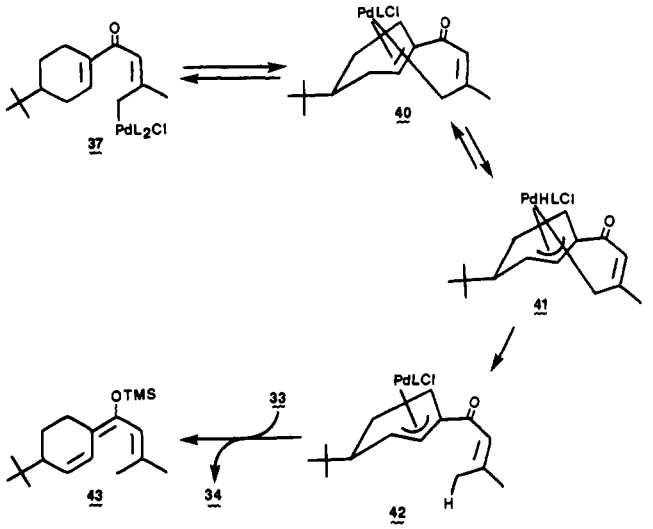
Scheme V. Proposed Mechanism for the Formation of **43**



deprotected starting materials (Scheme V). Triene **43** must have arisen by a hydride-transfer reaction. We envisage this as occurring via insertion of palladium across the axial C–H of coordinated complex **40** to form palladium(IV) hydride **41**.[43] Reductive elimination in the opposite direction generates allylpalladium(II) species **42**, which is incapable of undergoing intramolecular insertion processes. Trapping of palladium enolate **42** as before gives the observed silyl ether.

If the proposed mechanism for the SOH cyclization is correct, only hexatrienes possessing the necessary all-syn stereochemistry, or those capable of isomerization to that stereochemistry through allyl-palladium intermediates, can be utilized for the annulation (vide supra). To test the requirement for isomerization, known[44] *trans*-dienone **25** was converted into the kinetic silyl ether (LDA, TMSCl, 85%) and subjected to the SOH cyclization conditions (Table II, entry 7). Even after extended reaction times, no annulated material was observed and the silyl enol ether was returned unchanged in nearly quantitative yield. The lack of annulated product was due to the inability of the initially formed oxyallylpalladium complex to equilibrate in such a way as to isomerize to the necessary cis structure.

In summary, we have demonstrated three synthetically important concepts. First, it has been shown that the uncatalyzed thermal cyclization of dienone enolates or their TMS derivatives is not a facile process, suggesting that the electronic demands of the hexatriene cyclization run counter to the reactivity patterns of electron-rich hexatrienes. Second, the two-step cyclization of fully-conjugated and cross-conjugated dienones via [(trimethylsilyl)oxy]hexatrienes (SOHs) has been developed. Of the palladium complexes studied to date, $Pd(PFu_3)_2Cl_2$ is the optimal catalyst for the SOH cyclization. The methodology is not constrained by the stereochemistry about the hexatriene, as long as the palladium catalyst is able to act to equilibrate double-bond geometry. While the yield of annulated product varies with the structure of the SOH, it is important to note that starting material that does not afford annulated product is typically returned as deprotected [(trimethylsilyl)oxy]hexatriene. The palladium-catalyzed SOH cyclization, in combination with the Robinson annulation, allows placement of the carbonyl of an annulated cyclohexenone in three of the four possible positions on the newly formed ring (Scheme I), and synthetic flexibility is therefore extended. Cyclohexenone annulation via the palladium-catalyzed SOH cyclization is thus complementary to the Robinson annulation and promises to become a valuable addition to the arsenal of the synthetic organic chemist. Third, we have demonstrated a general principle for overcoming electronic barriers to electrocyclic reactions. Cyclization reaction pathways may be altered in unfavorable electronic cases through use of electron-poor (or electron-rich) transition-metal catalysts. We are currently studying the application of the SOH cyclization to the total synthesis of corticosteroids and extension of this reaction to phenol and heteroaromatic syntheses.

Experimental Section

^1H NMR spectra were obtained with $CDCl_3$ as solvent and tetramethylsilane as internal standard on Bruker WM-360 or AC-300 spectrometers. ^{13}C NMR spectra were recorded on Bruker WM-360 (91-MHz), AC-300 (75-MHz), or JEOL FX90Q (23-MHz) spectrometers with $CDCl_3$ as solvent and internal standard. ^{31}P NMR spectra were recorded on Bruker AC-300 (122-MHz) or JEOL FX90Q (36-MHz) spectrometers with $CDCl_3$ as solvent and 85% aqueous H_3PO_4 (0.0 ppm) or triphenylphosphine (−5.1 ppm) as external standard. Infrared spectra were taken on a Beckman Acculab 1 spectrometer. Capillary gas chromatographic analyses were run on a Hewlett-Packard 5890A gas chromatograph equipped with a 0.53 mm × 5 m methyl silicone column and a flame ionization detector. Low-resolution GC–mass spectra (LRMS) were obtained on a VG TRIO 1 instrument at an ionization potential of 70 eV. High-resolution mass spectra (HRMS) were obtained on a VG ZAB-HF mass spectrometer in the electron-impact mode. Fast atom bombardment mass spectra were obtained with a VG ZAB-HF mass spectrometer in the fast atom bombardment ionization mode with sulfolane as liquid matrix as previously described.[17] Elemental analyses were performed by Desert Analytics, Tucson, AZ. Thin-layer chromatography was performed on EM silica gel 60F-254 plates. Column chromatographic purification of reaction mixtures were performed with Woelm 230–400-mesh silica gel. Radial chromatography was performed on a Harrison Research Chromatatron.

1-Acetyl-2-vinylcyclohexene, 1-acetyl-2-((*E*)-hex-1-en-1-yl)cyclohexene, 1-acetyl-2-((*E*)-2-phenyl-1-ethenyl)cyclohexene, and 1-acetyl-2-phenylcyclohexene were prepared as previously described.[13] 1-((*E*)-3-Oxobut-1-en-1-yl)-4-*tert*-butylcyclohexene,[44] 4-*tert*-butylcyclohex-1-en-1-yl triflate,[45] 1-(tributylstannyl)-2-methylpropene,[46] $Pd(PPh_3)_4$,[47] tri-2-furylphosphine,[21] and tri-2-furylphosphine oxide[23] were prepared according to literature methods. Tetrahydrofuran (THF) was doubly distilled from potassium. 5,6,7,8-Tetrahydro-1-naphthol was purchased from the Aldrich Chemical Co. and used as a standard without further purification. Xylenes, toluene, dioxane, trimethylsilyl chloride, and triethylamine were freshly distilled from CaH_2. LiCl was dried at 140 °C for 24 h prior to use. All reactions were performed under positive argon pressure.

Dichlorobis(tri-2-furylphosphine)palladium(0) (15). To a solution of K_2PdCl_4 (1.28 g, 3.17 mmol) in water (30 mL) and acetone (5 mL) was added tri-2-furylphosphine (1.53 g, 6.49 mmol, 2.05 equiv). The resulting mixture was allowed to stir for 1 h and was extracted with CH_2Cl_2 (50 mL). The organic layer was washed with water (2 × 50 mL) and a saturated NaCl solution (2 × 50 mL), diluted with hexanes (100 mL), and cooled to 0 °C for 24 h. The resulting solids were collected and dried in an abderhalden apparatus (67 °C) to give **15** (0.75 g, 37%) as yellow crystals: IR (mineral oil mull) 3100, 1560, 1200, 1110, 890, 740 cm^{-1}; ^1H NMR (300 MHz) δ 6.41–6.42 (m, 1.14 H), 6.47–6.57 (m, 1.86 H), 7.03–7.05 (m, 1.14 H), 7.16–7.18 (m, 1.86 H), 7.53–7.55 (m, 1.14 H), 7.73–7.75 (m, 1.86 H); $^{13}C\{^1H\}$ NMR (75 MHz) δ 111.1–112.4 (m), 123.4–125.8 (m), 140.6–149.0 (m); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 121.5 MHz) δ −22.3 (s, 1.26 P), −29.1 (s, 0.74 P); FAB-MS (CH_2Cl_2/sulfolane, scanning range *m/z* 300–800) *m/z* (relative intensity, assignment) 726 (8, $Pd(PFu_3)_2Cl_2$ + sulfolane − HCl), 604 (95, $Pd(PFu_3)_2Cl_2$ − HCl), 570 (47, $Pd(PFu_3)_2Cl_2$ − 2 Cl), 503 (35, $Pd(PFu_3)_2Cl_2$ − 2 Cl − C_4H_3O), 338 (68, $Pd(PFu_3)_2Cl_2$ − 2 Cl −PFu_3). Anal. Calcd for $C_{24}H_{18}Cl_2O_6P_2Pd$: C, 44.50; H, 2.80. Found: C, 44.74; H, 2.95.

2-Vinyl-1-propionylcyclohexene (21). Dienone **21** was synthesized by a modification of a literature procedure.[13] To a solution of LiBr (0.66 g, 7.6 mmol, 1.5 equiv) and $Pd(PPh_3)_4$ (0.30 g, 0.26 mmol, 5.2 mol%) in THF (10 mL) was added a solution of 2-(mesyloxy)-1-propionyl-

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cyclohexene (1.2 g, 5.0 mmol) and vinyltributyltin (1.8 g, 5.5 mmol, 1.1 equiv) in THF (40 mL). The resulting mixture was heated to 80 °C for 48 h, cooled to room temperature, diluted with 1:1 ether/hexane (40 mL), and washed with water (50 mL). The aqueous layer was back-extracted with 1:1 ether/hexane (20 mL), and the combined organics were washed with a 10% NH_4OH solution (3 × 30 mL), water (2 × 30 mL), and a saturated NaCl solution (2 × 30 mL), dried (anhydrous $MgSO_4$), and filtered through a 3 × 2 cm pad of silica gel. Concentration under reduced pressure afforded a yellow oil that was purified by column chromatography (SiO_2, 2.5% ethyl acetate/hexane) followed by distillation to give **21** as a clear oil (0.42 g, 51%): bp (bulb-to-bulb) 78–85 °C (0.5 mmHg); TLC (5% EtOAc/hexane) R_f 0.27; IR (neat) 1680, 1560, 920 cm^{-1}; ^1H NMR (300 MHz) δ 1.09 (t, J = 7.3 Hz, 3 H), 1.67 (dt, J = 3.1, 6.2 Hz, 4 H), 2.26–2.28 (m, 4 H), 2.56 (q, J = 7.3 Hz, 2 H), 5.08 (d, J = 10.9 Hz, 1 H), 5.30 (d, J = 17.3 Hz, 1 H), 6.58 (dd, J = 10.9, 17.3 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75 MHz) δ 7.8 (q, J = 127.7 Hz), 21.8 (t, J = 128.2 Hz), 22.0 (t, J = 121.6 Hz), 24.6 (t, J = 122.8 Hz), 27.1 (t, J = 127.2 Hz), 35.2 (t, J = 123.3 Hz), 114.4 (t, J = 157.2 Hz), 134.7 (s), 135.2 (d, J = 153.6 Hz), 138.8 (s), 209.4 (s); LRMS m/z (relative intensity) 164 (33).

1-(4-*tert*-Butylcyclohex-1-en-1-yl)-3-methylbut-2-en-1-one (23). Dione **23** was synthesized with use of a modification of a literature procedure.[40,45] To a slurry of LiCl (1.05 g, 24.80 mmol, 5.08 equiv) and $Pd(PPh_3)_4$ (0.30 g, 2.61 mmol, 5.34 mol %) in dioxane (5 mL) was added a solution of 4-*tert*-butylcyclohex-1-en-1-yl triflate (1.40 g, 4.88 mmol) and 1-(tributylstannyl)-2-methylpropene (2.60 g, 7.53 mmol, 1.54 equiv) in dioxane (45 mL), followed by several crystals of BHT. The resulting solution was purged with CO for 10 min and then heated to 95 °C for 18 h. The resulting mixture was cooled to room temperature, diluted with a 1:1 ether/hexane mixture (35 mL), and washed with water (50 mL). The aqueous layer was back-extracted with a 1:1 ether/hexane mixture (20 mL), and the combined organics were washed with water (2 × 50 mL) and a saturated NaCl solution (2 × 50 mL), dried (anhydrous $MgSO_4$), and filtered through a 3 × 5 cm pad of silica gel. Concentration under reduced pressure afforded a yellow oil, which was purified by column chromatography (silica gel, 4 × 20 cm, 2.5% EtOAc/hexane) followed by distillation to give **23** (0.63 g, 58%): bp (bulb-to-bulb) 100–110 °C (0.4 mmHg); TLC (5% EtOAc/hexane) R_f 0.20; IR (neat) 1640, 1500, 840 cm^{-1}; ^1H NMR (300 MHz) δ 0.89 (s, 9 H), 1.01–1.10 (m, 1 H), 1.22–1.30 (m, 2 H), 1.91 (s, 3 H), 2.06 (s, 3 H), 2.00–2.35 (m, 4 H), 6.41 (s, 1 H), 6.84 (t, J = 2.6 Hz, 1 H); $^{13}C\{^1H\}$ NMR (23 MHz) δ 20.6, 23.4, 24.7, 27.0, 27.4, 27.6, 32.0, 43.4, 120.8, 139.0, 140.5, 152.2, 192.7; LRMS m/z (relative intensity) 220 (M^+, 12%); HRMS for $C_{15}H_{24}O$, calcd 220.1870, found 220.1834.

General Procedure for Cyclization of [(Trimethylsilyl)oxy]hexatrienes. $\Delta^{5(10)}$-Bicyclo[4.4.0]decen-2-one (13). To a solution of LDA [diisopropylamine (0.60 mL, 4.28 mmol, 2.12 equiv), *n*-butyllithium (2.0 mL, 1.86 M in hexane, 3.72 mmol, 1.84 equiv)] in THF (50 mL) at −78 °C was added a solution of dienone **11** (0.30 g, 2.02 mmol) in THF (25 mL). The resulting enolate was maintained at −78 °C for 10 min, then treated with a mixture of trimethylsilyl chloride (0.80 mL, 6.30 mmol, 3.12 equiv) and triethylamine (1.40 mL, 10.04 mmol, 3.12 equiv), and allowed to warm to room temperature. The resulting solution was concentrated under reduced pressure to afford an oil that was triturated with hexanes (20 mL), filtered through a 3 × 5 cm pad of Celite, concentrated under reduced pressure, and purified by distillation to give **12** (0.44 g) as a clear oil: bp (bulb-to-bulb) 85–95 °C (0.5 mmHg); IR (neat) 1610, 1250, 1120, 840 cm^{-1}; ^1H NMR (360 MHz) δ 0.16 (s, 9 H), 1.29–1.62 (m, 4 H), 2.12 (br s, 2 H), 2.34 (br s, 2 H), 4.32 (s, 1 H), 4.54 (s, 1 H), 5.01 (d, J = 11.0 Hz, 1 H), 5.17 (d, J = 17.5 Hz, 1 H), 7.34 (dd, J = 11.0, 17.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR (91 MHz) δ 0.3 (3 C), 22.7, 22.8, 25.1, 29.1, 95.8, 132.1, 136.8, 137.3, 157.0; LRMS m/z (relative intensity) 222 (M^+, 4%). Silyl enol ether **12** was greater than 95% pure as determinated by ^1H and ^{13}C NMR and GC analysis. This material was used for cyclization without further purification.

A mixture of silyl trienol ether **12** (0.11 g, 0.50 mmol) and $Pd(PFu_3)_2Cl_2$ (0.017 g, 0.026 mmol, 5.12 mol %) in xylenes (15 mL) was heated at the reflux temperature for 36 h and then cooled to room temperature. The resulting black slurry was concentrated under reduced pressure, diluted with a 1:1 ether/hexane solution (25 mL), washed with water (2 × 20 mL) and saturated brine (2 × 20 mL), dried (anhydrous $MgSO_4$), filtered through a 3 × 5 cm pad of silica gel, and concentrated under reduced pressure to give a yellow oil. This was purified by chromatography (SiO_2, 1-mm chromatotron plate, 5% EtOAc/hexane) to give enone **13** as a colorless oil (0.053 g, 70%): bp (bulb-to-bulb) 69–75 °C (0.5 mmHg) [lit.[48] bp 95 °C (0.8 mmHg)]; TLC (5% EtOAc/hexane) R_f 0.13; IR (neat) 2920, 1650 cm^{-1}; ^1H NMR (360 MHz) δ 1.61–1.63 (m, 4 H), 1.95 (tt, J = 6.4, 6.4 Hz, 2 H), 2.18–2.24 (m, 6 H), 2.38–2.41 (t, J = 6.7 Hz, 2 H); $^{13}C\{^1H\}$ NMR (75 MHz) δ 22.1 (t, J = 126.2 Hz), 22.2 (t, J = 128.0 Hz), 22.4 (t, J = 126.9 Hz), 22.9 (t, J = 128.5 Hz), 31.4 (t, J = 124.5 Hz), 31.8 (t, J = 124.6 Hz), 37.9 (t, J = 127.7 Hz), 132.3 (s), 156.9 (s), 199.1 (s); LRMS m/z (relative intensity) 150 (M^+, 34%). Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 80.09, H, 9.37. ^1H and ^{13}C NMR and IR spectra of **13** were identical with those previously reported.[48]

$\Delta^{5(10)}$-3-Butylbicyclo[4.4.0]decen-2-one (17): bp (bulb-to-bulb) 90–110 °C (0.4 mmHg); TLC (5% EtOAc/hexane) R_f 0.13; IR (neat) 2950, 1660, 1635 cm^{-1}; ^1H NMR (360 MHz) δ 0.88 (t, J = 6.5 Hz, 3 H), 1.30–1.35 (m, 6 H), 1.49–1.56 (m, 2 H), 1.66–1.71 (m, 2 H), 2.02–2.10 (m, 3 H), 2.18–2.20 (m, 2 H), 2.23–2.29 (m, 2 H), 2.50 (d, J = 12.7 Hz, 2 H); $^{13}C\{^1H\}$ NMR (75 MHz) δ 13.9 (q, J = 124.4 Hz), 21.9 (t, J = 123.2 Hz), 22.0 (t, J = 127.7 Hz), 22.6 (t, J = 123.0 Hz), 28.6 (t, J = 127.3 Hz), 31.7 (t, J = 125.8 Hz), 34.4 (d, J = 122.7 Hz), 35.5 (t, J = 123.1 Hz), 38.0 (t, J = 126.8 Hz), 44.2 (t, J = 124.9 Hz), 131.8 (s), 156.0 (s), 199.2 (s); LRMS m/z (relative intensity) 206 (M^+, 46%). Anal. Calcd for $C_{14}H_{22}O$: C, 81.49; H, 10.75. Found: C, 80.25, H, 9.98.

$\Delta^{5(10)}$-3-Phenylbicyclo[4.4.0]decen-2-one (19): bp (bulb-to-bulb) 100–115 °C (0.5 mmHg); TLC (5% EtOAc/hexane) R_f 0.14; IR (neat) 3040, 1660, 1500, 730 cm^{-1}; ^1H NMR (360 MHz) δ 1.52–1.60 (m, 2 H), 1.69–1.78 (m, 2 H), 2.13–2.36 (m, 2 H), 2.40–2.51 (m, 2 H), 2.59–2.72 (m, 4 H), 3.23–3.31 (m, 1 H), 7.21–7.24 (dd, J = 6.74, 6.17 Hz, 2 H), 7.30–7.32 (d, J = 6.74 Hz, 2 H), 7.32–7.34 (d, J = 6.17 Hz, 1 H); $^{13}C\{^1H\}$ NMR (75 MHz) δ 22.0 (t, J = 127.6 Hz), 31.9 (t, J = 126.8 Hz), 39.2 (t, J = 128.0 Hz), 40.3 (d, J = 128.2 Hz), 44.4 (t, J = 129.2 Hz), 126.5 (dm, J = 153.2 Hz), 126.6 (dd, J = 151.1, 7.16 Hz), 128.5 (dd, J = 159.8, 7.5 Hz), 132.0 (s), 143.5 (s), 155.8 (s), 198.3 (s); LRMS m/z (relative intensity) 226 (M^+, 51%). Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.06. Found: C, 84.81; H, 7.94.

3-Methyl-7-*tert*-butylbicyclo[4.4.0]dec-2-enone (24c and 24t). To a solution of LDA [diisopropylamine (0.35 mL, 2.5 mmol, 3.31 equiv), *n*-butyllithium (0.60 mL, 2.65 M in hexane, 1.54 mmol, 2.04 equiv)] in THF (20 mL) at −78 °C was added a solution of dienone **23** (0.17 g, 0.76 mmol) in THF (10 mL). The resulting enolate was stirred at −78 °C for 10 min and then treated with a mixture of trimethylsilyl chloride (0.60 mL, 4.73 mmol, 6.26 equiv) and triethylamine (1.00 mL, 7.17 mmol, 9.50 equiv) and allowed to warm to room temperature. The resulting solution was concentrated under reduced pressure to afford an oil that was triturated with hexanes (20 mL), filtered through a 3 × 5 cm pad of basic alumina, and concentrated under reduced pressure to give silyl trienol ether **33** (0.18 g, 83%) as a clear oil: bp (bulb-to-bulb) 105–110 °C (0.25 mmHg); ^1H NMR (C_6D_6, 360 MHz) δ 0.20 (s, 9 H), 0.80 (s, 9 H), 0.90–1.45 (m, 5 H), 1.68–1.41 (m, 1 H), 2.00 (s, 3 H), 2.00–2.19 (m, 1 H), 5.01 (br s, 1 H), 5.34 (br s, 1 H), 5.42 (s, 1 H), 6.15 (t, J = 2.7 Hz, 1 H). Silyl enol ether **33** was determined to be one isomer of greater than 95% purity by ^1H NMR and GC analysis. This material was used for cyclization without further purification.

A mixture of silyl trienol ether **33** (0.0504 g, 0.172 mmol) and $Pd(PFu_3)_2Cl_2$ (0.0119 g, 0.0184 mmol, 10.7 mol %) in toluene (12 mL) was heated at the reflux temperature for 7 days and then cooled to room temperature. The resulting black slurry was concentrated under reduced pressure, diluted with a 1:1 ether/hexane solution (25 mL), washed with water (2 × 20 mL) and saturated brine (2 × 20 mL), dried (anhydrous $MgSO_4$), filtered through a 3 × 5 cm pad of silica, and concentrated under reduced pressure. The resulting yellow oil was separated by chromatography (SiO_2, 1-mm chromatotron plate, 5% EtOAc/hexane) to give deprotected starting material **23** (0.105 g, 61%), followed by **24t** (0.0047 g, 12%) and then **24c** (0.0081 g, 22%).

24t: mp 48–50 °C; bp (bulb-to-bulb) 90–110 °C (0.5 mmHg); TLC (5% EtOAc/hexane) R_f 0.11; IR (neat) 2980, 1670, 840 cm^{-1}; ^1H NMR (360 MHz) δ 0.85 (s, 9 H), 0.89–1.03 (m, 5 H), 1.25–1.35 (m, 2 H), 1.56–1.59 (m, 2 H), 1.92 (s, 3 H), 2.13–2.23 (m, 2 H), 2.27–2.35 (m, 1 H), 5.84 (s, 1 H); $^{13}C\{^1H\}$ NMR (91 MHz) δ 24.2, 25.8, 26.6, 27.5, (3 C), 28.9, 29.7, 32.3, 39.2, 47.1, 49.9, 126.3, 160.8, 201.3; LRMS m/z (relative intensity) 220 (22).

24c: bp (bulb-to-bulb) 90–110 °C (0.5 mmHg); TLC (5% EtOAc/hexane) R_f 0.05; IR (neat) 2980, 1670, 840 cm^{-1}; ^1H NMR (360 MHz) δ 0.86 (s, 9 H), 0.96–0.99 (m, 1 H), 1.20–1.30 (m, 6 H), 1.42–1.44 (m, 2 H), 1.55–1.73 (m, 1 H), 1.96 (s, 3 H), 2.38–2.55 (m, 1 H), 5.82 (s, 1 H); $^{13}C\{^1H\}$ NMR (91 MHz) δ 24.4, 25.4, 26.4, 27.5 (3 C), 30.4, 32.3, 32.5, 33.7, 41.8, 47.9, 125.2, 161.7, 203.6; LRMS m/z (relative intensity) 220 (9).

In a separate experiment, treatment of silyl trienol ether **33** (0.34 g, 1.16 mmol) with $(PFu_3)_2Cl_2$ (0.38 g, 0.59 mmol, 5.04 mol %) in toluene (20 mL) for 36 h, followed by the standard workup and chromatography (SiO_2, 1-mm chromatotron plate, 5% EtOAc/hexane), gave isomerized silyl trienol ether **43** (0.083 g, 24%) as a mixture of isomers, followed by

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deprotected starting material **23** (0.11 g, 43%) and a mixture of **24t** and **24c** (0.054 g, 21%).

43: TLC (5% EtOAc/hexane) R_f 0.34; IR (neat) 3020, 1610, 1250, 1210, 1075, 1030, 880, 845 cm^{-1}; ^1H NMR (360 MHz) δ 0.17 (s, 9 H), 0.92 (s, 9 H), 1.68 (d, J = 1.1 Hz, 3 H), 1.81 (d, J = 1.4 Hz, 3 H), 2.82 (dt, J = 15.3, 3.7 Hz, 1 H), 5.62 (d, J = 10.1 Hz, 1 H), 5.68 (br s, 1 H), 6.06 (dd, J = 10.3, 2.3 Hz, 1 H); LRMS m/z (relative intensity) 292 (5). Silyl trienol ether **42** was approximately 75% pure as determined by ^1H and ^{13}C NMR and GC analyses. Contaminants included a stereoisomer [13% by GC; LRMS m/z (relative intensity) 292 (7)] and two unidentified components.

Note Added in Proof

Fehr reported that (trimethylsilyl)oxy derivatives of *all-cis*-hexatrienes undergo cyclization under pyrolysis conditions (0.8 mL/min, 365 °C) but that the trans isomers were returned unchanged.[49] These results are consistent with our observation that the thermal cyclization of SOH **12** proceeds very slowly at 110 °C.

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Synthesis, Structure, and Properties of a 2-(Trimethylsilyl)cyclobutenocyclooctatetraene

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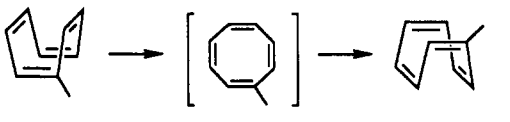
Abstract: The first example of the cyclobutenocyclooctatetraene structural class (**2**) to possess stability at room temperature has been prepared by a route involving ring contraction via a Wolff rearrangement. Derivatives have been characterized by various spectroscopic techniques, X-ray crystallography, and cyclic voltammetry. All of these properties are in concert with a structure possessing a high-lying HOMO, low-lying LUMO and a carbon skeleton closer to planarity than any bicyclic cyclooctatetraene yet prepared.

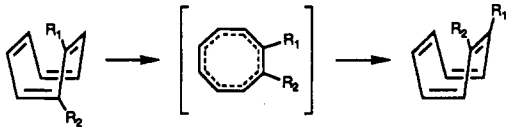
Introduction

Cyclooctatetraene has drawn attention as the vinylog of benzene since it was first prepared by Willstatter in 1911.[2] This interest was further intensified by Huckel's 1937 proposal[3] that a 4n π-electron system, such as is superficially present in cyclooctatetraene, should possess an unfavorable electronic delocalization. That cyclooctatetraene itself could exist as a stable molecule yet not violate this canon was made explicable by its structural characterization as a nonplanar "tub" form[4] possessing alternating double and single bonds.[5]

Two approaches have been taken to reveal possible 4n cyclic conjugation in cyclooctatetraenes, both involving synthesis of analogues. The first is based on the known isomerizations of cyclooctatetraenes, for which two modes are available because of their nonplanarity and alternating bonds. Ring inversion (eq 1) relates to conformational mobility and enantiomerization and can proceed through a planar D_{4h} transition state with alternating bonds. Extensive measurements on the inversion barriers of cyclooctatetraenes have been made.[6] Bond shifting (eq 2) relates



(1)



(2)

to *constitutional isomerism* and for the most part has a higher activation energy than inversion.[6,7] While it seems intrinsic that the transition state for bond shifting is fully conjugated, recent

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