Spiro-Fused 2,5-Cyclohexadienones from Thermal 1,3-Shifts in Quinol Vinyl Ethers. Reactions in Nonbenzenoid Systems and Limitations of the Chemistry

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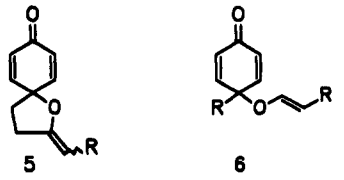
Addition of functionalized organolithium compounds to quinone monoketals furnished 4-hydroxy-2,5-cyclohexadienone derivatives. The 4-hydroxyl group of these molecules was then transformed into a vinyl ether, and the thermal [1,3]-shift chemistry of these functionalized vinyl ethers was studied. In dienone derivatives wherein a [3,3]-sigmatropic shift was not stereoelectronically possible, these molecules underwent thermal and photochemical [1,3]-oxygen-to-carbon migration, affording spiro-2,5-cyclohexadienones in good yield. However, for compounds in which the [3,3]-shift involving the vinyl ether was possible, this reaction occurred at or below room temperature. 1,5-Cyclooctadienebis(methyldiphenylphosphine)iridium hexafluorophosphate was found to be an especially efficient catalyst for the allyl-to-vinyl ether isomerization in these systems.

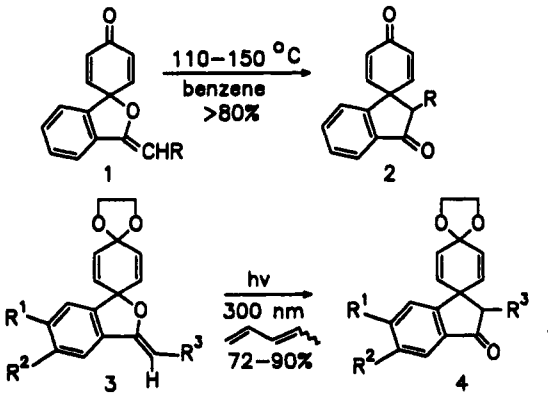
Introduction

Quinone monoketals, readily available from anodic oxidation of 1,4-dioxygenated benzene derivatives followed by mild acidic hydrolysis, possess a high density of functional groups and are versatile synthetic intermediates.[1] We recently reported that quinol vinyl ethers prepared from quinone monoketals can be converted thermally[2] and photochemically[3] to spiro-fused 2,5-cyclohexadienones (Scheme I). These compounds were chosen to avoid competition between the [3,3]- and [1,3]-sigmatropic shifts and the known difficulties associated with vinyl ether preparations.[4] Two questions of general interest concern the 1 → 2 transformation outlined in Scheme I. First, how does the aromatic ring influence the facility of the [1,3]-shift reaction? Second, could the [1,3]-shift compete with a [3,3]-shift in compounds in which both reactions are stereoelectronically possible? A study of the thermal chemistry of compounds analogous to 5 and 6 would furnish information on the two points noted above.

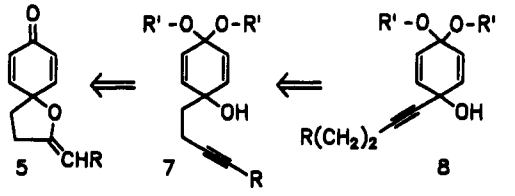


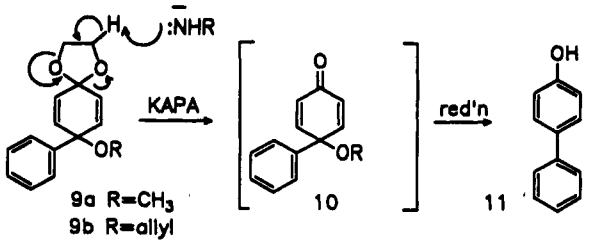
Synthesis of α-Methylene Cyclic Ethers and Their [1,3]-Shift Chemistry. First, the preparation of vinyl ethers analogous to 5 was studied, employing the general route outlined in Scheme II. The monoethylene ketal of benzoquinone was studied first because the ethylene ketal would be less subject to ketal hydrolysis by adventitious acid in subsequent chemistry than would be the dimethyl ketal.[5] Although the alcohol analogous to 8 (ethylene ketal, R = H) was prepared from 1-lithiobutyne and the ethylene monoketal of benzoquinone, the potassium 3-aminopropylamide (KAPA)[6] mediated isomerization of the internal acetylene to the terminal acetylene (8 → 7) was not successful. The products from this reaction were not characterized; however, the reaction of **9a,b** with KAPA under similar conditions led to *p*-phenylphenol in 35% and 40% yields, respectively. The failure of the *acetylene zipper reaction* with the compounds having an ethylene ketal is probably related to the fragmentation shown below.[7]

Scheme I. Thermal and Photochemical [1,3]-Shift Routes to Spirodienones



Scheme II. General Route to Spirocyclic Vinyl Ethers





(1) For reviews and leading references, see: (a) Swenton, J. S. *Acc. Chem. Res.* **1983**, *16*, 74. (b) Swenton, J. S. In *Chemistry of Quinones, Part 2*; Rappoport, Z., Patai, S., Eds.; John Wiley: New York, 1988; p 899.

(2) (a) Wang, S.; Morrow, G. W.; Swenton, J. S. *J. Org. Chem.* **1989**, *54*, 5364. (b) Morrow, G. W.; Wang, S.; Swenton, J. S. *Tetrahedron Lett.* **1988**, *29*, 3441.

(3) Wang, S.; Callinan, A.; Swenton, J. S. *J. Org. Chem.* **1990**, *55*, 2272.

(4) The literature records difficulties associated with the preparation of α-methylene cyclic ethers. Ireland, R. E.; Habich, D.; Norberck, D. W. *J. Am. Chem. Soc.* **1985**, *107*, 3271 and references cited therein. Pale, P.; Chuche, J. *Tetrahedron Lett.* **1988**, *29*, 2947.

(5) (a) For preparation of the ethylene ketal of benzoquinone, see: Dolson, M. G.; Swenton, J. S. *J. Org. Chem.* **1981**, *46*, 177. (b) The ethylene ketal hydrolyzes 300–500 times slower than does the dimethyl ketal in these systems: Stern, A. J.; Swenton, J. S. *J. Org. Chem.* **1989**, *54*, 2953.

(6) (a) Brown, C. A.; Yamashita, A. *J. Am. Chem. Soc.* **1975**, 891–892. (b) Abrams, S. R.; Shaw, A. C. *Organic Synthesis*; New York: Wiley, 1987; Collect. Vol. 66, p 127.

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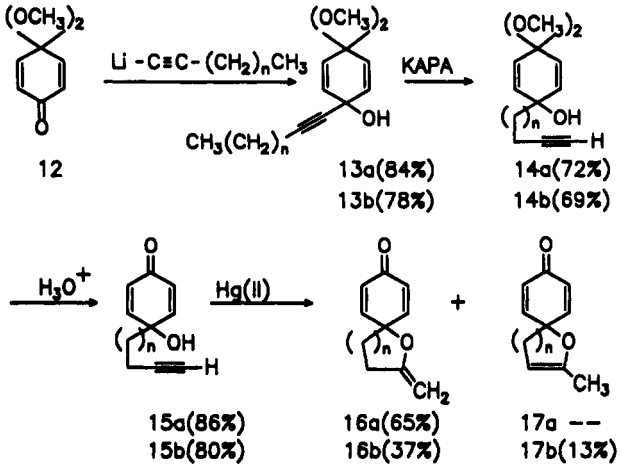
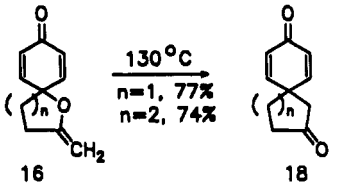
Scheme III. Synthesis of α-Methylene Spirocyclic Ethers

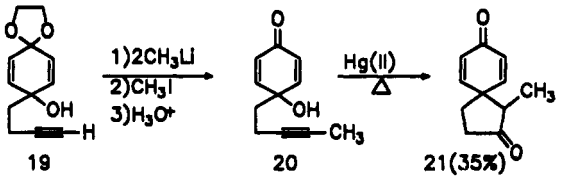


While this approach to **5** using the ethylene ketal failed, a similar reaction sequence using the dimethyl ketal was successful. The reaction sequence outlined in Scheme III performed with 1-butyne and 1-pentyne furnished both **15a** and **15b**. Mercury(II)-catalyzed cyclization of these hydroxy acetylenes gave sufficient amounts of the α-methylene cyclic ethers **16a,b** for the studies here; however, the preparations were very sensitive to reaction conditions. The main complication associated with the chemistry is the facile isomerization of the exocyclic isomers **16** to the endocyclic isomers **17** during the cyclization reaction.[4] This isomerization was especially troublesome in the preparation of **16b** and required that the **15b** → **16b** reaction be conducted only to ≤50% conversion. Additionally, isomerization occurs on chromatography so the separations must be performed rapidly on base-washed silica gel.

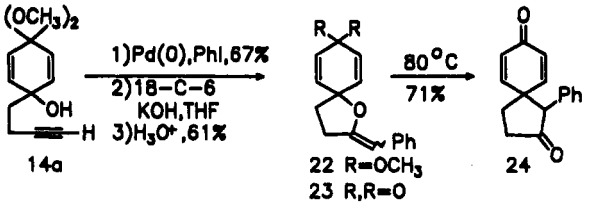
The thermal rearrangements of the exocyclic vinyl ethers **16a,b** were conducted in degassed benzene at 130 °C and furnished the known spirocyclic dienones **18a** (77%) and **18b** (74%). The kinetics for the isomerization of **16a** were studied at 130 °C, and the average rate constant for conversion to **18a** was 1.5×10^{-4} s^{-1}. This is 50 times faster than the rearrangement[2a] of the benzo analogue **1** (R = H) and indicates that the aromatic ring in **1** slows the rate of the [1,3]-shift process.



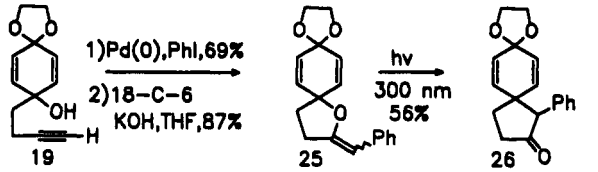
Two other compounds were also prepared, and their thermal chemistry was studied. The acid-catalyzed reaction of **14a** with ethylene glycol resulted in ketal exchange, affording **19** (88%). Standard transformations then afforded the hydroxy acetylene derivative **20**. Formation of the pure exocyclic vinyl ether was even more difficult for this compound, so vinyl ether formation from **20** was performed in xylene at reflux with the hope that the vinyl ether formed in situ would undergo the [1,3]-shift faster than isomerization to the endocyclic vinyl ether. The isolation of **21** (35%) verified this expectation since this is approximately the combined yield for vinyl ether formation and [1,3] rearrangement observed in the reactions described above.



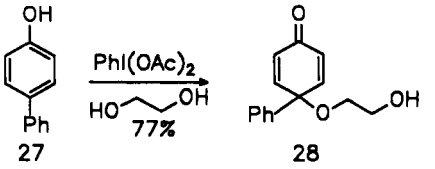
In our previous studies,[2a] phenyl substitution on the terminal carbon of the vinyl ether accelerated the thermal [1,3]-shift reaction; a similar effect was noted here. The phenyl-substituted compound was prepared as outlined below. The cyclization of the hydroxyphenylacetylene to the vinyl ether **22** using potassium hydroxide and 18-crown-6 was especially convenient for the preparation of **23** and **25**. In neither case was the endocyclic isomer detected. This method may be a general method for preparation of α-methylene cyclic ethers for molecules which do not have a base-labile substituent. Heating the vinyl ether **23** in benzene (≤80 °C) gave the spirocyclic diketone **24** (71%).



The phenyl-substituted vinyl ether **25** had a convenient chromophore for exploring the photochemical version of the [1,3]-shift in these systems. Indeed, irradiation of **25** gave **26** (56%). Although the yield is somewhat less than those observed in the related benzosystems[3] (i.e., **3** → **4**), the reaction conditions were not optimized for this reaction. Thus, for compounds having a chromophore in the ultraviolet region, effecting the [1,3]-shift photochemically in these systems will afford a diketone with one of the carbonyl groups protected as a ketal.



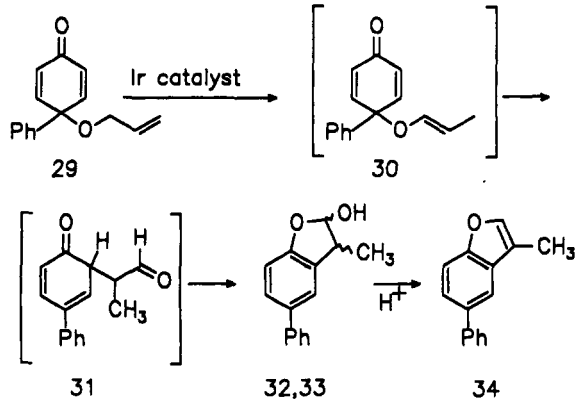
Preparation of Noncyclic Vinyl Ethers. The question of competition between the [1,3]-shift and the [3,3]-shift could be answered by studying the chemistry of compounds analogous to **6**. Our first attempt to obtain vinyl ethers of this type involved the quinol ether **28** prepared via an interesting oxidative addition of ethylene glycol to *p*-phenylphenol. However, a number of attempts—elimination of the mesylate with various bases, *o*-nitrophenyl selenoxide elimination,[8] the Hoffmann elimination of the quaternary amine—to effect elimination of water from **28** to form the vinyl ether were unsuccessful.



(7) For leading references to related base-catalyzed fragmentations see ref 6 in: Spangler, L. A.; Swenton, J. S. *J. Org. Chem.* **1984**, *49*, 1800.

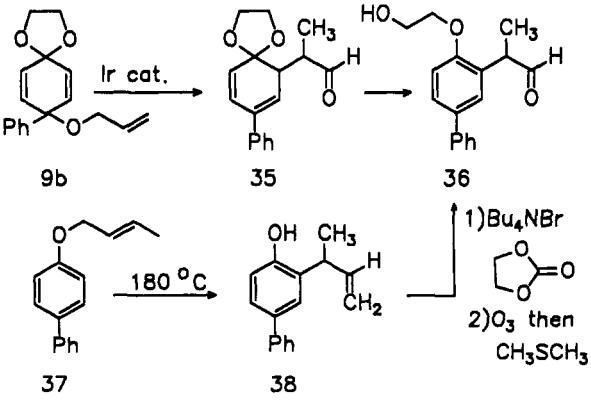
(8) Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947. Grieco, P. A.; Nishizawa, M. *Ibid.* **1977**, *47*, 1717.

A second approach involved formation of an allyl ether followed by isomerization of the allyl ether to a vinyl ether. While a number of procedures have been used to effect this isomerization, the high density of functionality in **29** led



to problems with some of these methods.[9] For example, the reaction of **29** with *bis*(triphenylphosphine)rhodium chloride gave *p*-phenylphenol (45%) as the major product. Finally, the reaction of **29** with $[(C_8H_{12})Ir(PMePh_2)_2]PF_6$[10] at room temperature afforded a clean reaction. However, the product was not the expected vinyl ether but rather a mixture of hemiacetals **32** and **33**. Reaction of the mixture with *p*-TsOH gave the benzofuran **34**. The results of the reaction of **29** with the iridium catalyst appear to involve isomerization of **29** to the vinyl ether **30**, a room-temperature Claisen rearrangement to **31**, followed by aromatization and hemiacetal formation. *The facility of the [3,3]-shift in this system was surprising.*

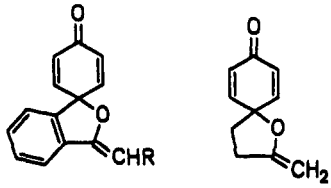
The ethylene ketal system was studied next since it was known that substitution of the ketal for the ketone moiety in **1** markedly lowers the rate of thermal rearrangement. If this held for the [3,3]-shift process and vinyl ether analogous to **30** could be isolated, then photochemical activation of the vinyl ether would give the desired [1,3]-shift product. However, the reaction of **9b** did not lead to the desired vinyl ether but rather to **35**, a product derived from a room temperature [3,3]-rearrangement. The ketal **35** was aromatized by reaction with acid to afford **36**. The structure of this latter compound was unequivocally established by comparison with synthesized material (see below and in the supplementary material).



To establish that the allyl-to-vinyl ether isomerization was possible with *tertiary* ethers of the type studied here,

(9) *Protecting Groups in Organic Synthesis*; Greene, T., Eds.; John Wiley & Sons: New York, 1981; pp 27–28.
(10) Baudry, D.; Ephritikhine, M.; Felkin, H. *J. Chem. Soc., Chem. Commun.* **1978**, 694. Oltvoort, J. J.; van Boeckel, C. A. A.; De Koning, J. H.; van Boom, J. H. *Synthesis* **1981**, 305.

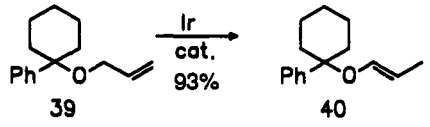
Chart I. Relative Rates of [1,3]-Shifts of Vinyl Ethers



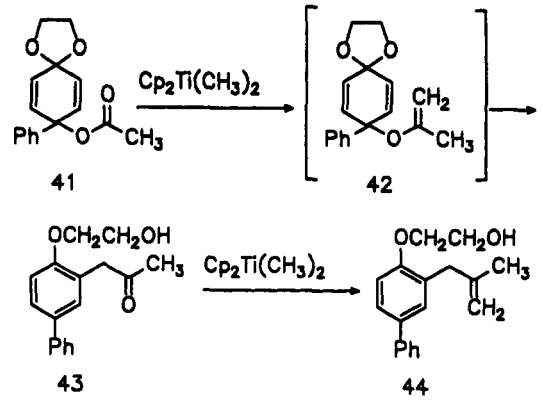
1[a] (R = H)
15[b] (R = CH_3)
200[b] (R = Ph)

[a] Relative to 1 at 130 °C. [b] Relative to 1 at 153 °C.

the simple allyl ether **39** was studied. Reaction of **39** with the iridium catalyst at room temperature gave the vinyl ether **40** (93%). Thus, there appears little doubt that the desired allyl to vinyl ether isomerization is occurring in compounds **29** and **9b**.



There was the possibility that the iridium catalyst used for the allyl-to-vinyl ether conversion was catalyzing the [3,3]-shift. Thus, a second approach was investigated for preparation of vinyl ethers analogous to **30**. Reaction of **41** with dimethyltitanocene[11] in toluene at 75 °C afforded a mixture of **43** and **44**. If an excess of dimethyltitanocene was employed in the reaction, **44** was formed (53%). Although this chemistry did not proceed at a satisfactory rate at room temperature, the formation of **43** at 75 °C confirms the facile [3,3]-shift in these systems.



Discussion

The [1,3]-oxygen-to-carbon shift reaction of vinyl ethers serves as a convenient method for formation of quaternary carbon–carbon bonds in 2,5-cyclohexadienones. The limitations of the reaction arise from competition of the [1,3]-shift reaction with the orbital symmetry-allowed [3,3]-shift. In the investigated cases, it was not possible to isolate vinyl ethers when the molecules were capable of undergoing the [3,3]-shift. While the [1,3]-shift chemistry can be conducted in good yield for compounds **16a,b** to form spirocyclic ketones, current methods for preparation of the vinyl ethers detract from the synthetic utility of the reaction.

Although the mechanism of the [1,3]-shift reaction has not been established, the effect of substituents on the rate

(11) Petasis, N. A.; Bzowej, E. I. *J. Am. Chem. Soc.* **1990**, *112*, 6392.

of these vinyl ether rearrangements has been further clarified by these studies. Chart I summarizes the effect of substituents on the rate of the [1,3]-shift. The absence of the benzene ring in **16a** actually increases the rate of rearrangement by a factor of 50 at 130 °C. The carbon–oxygen bond undergoing cleavage in the transition state is nearly orthogonal to the aromatic ring, so an aryl ring would impart little resonance stabilization to the bond-breaking process. Additionally, the ρ value –0.85 for the [1,3]-shift in phenyl-substituted systems[2a] indicates that the reaction is aided by donating substituents. Perhaps the slower rate for the benzenoid compound **1** versus **16a** is related to the inductive effect of the sp^2 carbons in the aromatic ring of **1**. The results are most consistent with rate-determining cleavage of the *tertiary* carbon–oxygen bond of the quinol vinyl ether followed by carbon–carbon bond formation between the phenoxy and vinyloxy radical segments.

Experimental Section[12]

3,3,6,6-Tetramethoxycyclohexa-1,4-diene. The following two procedures are convenient preparations of the bis- and monomethyl ketals of benzoquinone. The anodic oxidation of 1,4-dimethoxybenzene (100 g, 0.68 mol) in 2% methanolic KOH (600 mL) was performed in a stirred water-jacketed beaker at 15–20 °C using a cylindrical platinum mesh anode (45 mesh, 1.5 in. diameter × 2 in. high) and a platinum sheet cathode (0.5 × 0.5 in.) at a current of 2 amp. Initially, the solution was heterogeneous but became homogeneous after about 2 h of electrolysis. The progress of the reaction can be monitored by either GC (OV-101 on 100/120 mesh Chrom G H-P, 20 × 1/8 in. diameter, 110 °C) or UV spectroscopy at 290 nm. The reaction was judged to be complete after 24 h, and the yellow-orange reaction mixture was concentrated in vacuo. The resulting residue was dissolved in hot water (100 mL) and then rapidly swirled in an ice bath to crystallize the product. Filtration gave a light yellow solid, which was then washed with ice–water (150 mL) to give a white crystalline solid. Drying the material under vacuum (1 mmHg) in a Kugelrohr apparatus gave white crystalline product (105 g, 73%). This bisketal (mp 43–45 °C, lit.[13] mp 42.5 °C) showed a ^{1}H NMR spectrum identical with that of the known compound. Additional material could be obtained from extractive workup of the filtrate.

4,4-Dimethoxycyclohexa-2,5-dienone (12). To a 4:1 acetone/water (500 mL) solution of the above bisketal (80 g, 0.4 mol) at 24 °C was added glacial HOAc until pH ≃5. The pH was monitored by a pH electrode and ranged between 4.6 and 5.0 during the hydrolysis. The progress of the reaction was followed by GC (OV-101 on 100/120 mesh Chrom G H-P, 20 × 1/8 in. diameter, 110 °C) and was judged to be complete after 3.5 h. After addition of $NaHCO_3$ to raise the pH to 7, the majority of the solvent was removed in vacuo, and the residue was extracted with Et_2O (3 × 200 mL). The combined ether layers were washed with 1% KOH (2 × 100 mL), and the resulting light yellow ethereal layer was worked up as usual. Kugelrohr distillation (80–100 °C bath (1 mmHg) gave **12** as a light yellow liquid (58 g, 93%), which was pure by ^{1}H NMR spectroscopy. Alternatively, the product can be vacuum distilled [bp 85–89 °C (7–9 mmHg) (lit.[14] bp 70–73 °C (0.7 mmHg))]; however, some decomposition during distillation has been noted.

4-(1-Butynyl)-4-hydroxycyclohexa-2,5-dienone Dimethyl Acetal (13a). Gaseous 1-butyne (0.06 mol, 5.6 mL) was condensed at –78 °C into a graduated test tube and was then bubbled into a solution of BuLi (1.5 M, 48 mL, 0.05 mol) in Et_2O (100 mL) at –78 °C. The solution was warmed to 0 °C for 15 min, during which time butane evolved and the acetylide precipitated. The resulting heterogeneous suspension was cooled to –78 °C, and **12** (5.90 g, 0.038 mol) was added dropwise. The solution immediately turned deep blue, and after 5 min the solution was allowed to warm to 0 °C. After 1 h, the color of the solution had turned from blue to colorless, and the reaction was quenched by addition of H_2O (25 mL). Extractive workup with Et_2O (3 × 100 mL) gave **13a** (7.74 g, 97%) as a brown oil that was ≃90% pure by ^{1}H NMR spectroscopy. This material was sufficiently pure for subsequent chemistry and could not be obtained analytically pure easily. Material of ≃98% purity could be obtained as described below. The crude oil was dissolved in CH_3OH (20 mL) and cooled to 0 °C, and $NaBH_4$ (0.3 g) was added. After 0.5 h, the CH_3OH was removed in vacuo, and the solution was made basic by adding 5% NaOH. Extractive workup with Et_2O (2 × 50 mL) gave **13a** (6.7 g, 84%) as a clear, nearly colorless oil, >98% pure by ^{1}H NMR spectroscopy: ^{1}H NMR δ 5.94 (AB q, $\Delta\nu$ = 28 Hz, J = 10 Hz, 4 H), 3.21, 3.19 (overlapping s, 6 H), 2.13 (q, J = 8 Hz, 2 H), 1.04 (t, J = 8 Hz, 3 H); IR (NaCl, cm^{-1}) 3400, 2970, 2940, 2220 (w), 1100, 1060, 1030, 950; HRMS calcd for $C_{12}H_{16}O_3$ m/e 208.1100, obsd 208.1087.

4-(3-Butynyl)-4-hydroxycyclohexa-2,5-dienone Dimethyl Acetal (14a). To an evacuated flask containing KH (3 g, 0.075 mol) that was previously washed with hexane and dried in vacuo was added 1,3-diaminopropane (50 mL). Evolution of H_2 was rapid at first, slowed down after about 5 min, and was complete after 5 h. Then the flask was cooled to 0 °C, and a solution of *p*-quinol ketal **13a** (2.5 g, 0.012 mol) in 1,3-diaminopropane (7 mL) was added dropwise. After 5 min, the solution was poured into ice–water (300 mL). Extractive workup with CH_2Cl_2 (4 × 100 mL) gave **14a** (1.8 g, 72%) as a light brown oil that was >95% pure by ^{1}H NMR spectroscopy. A small sample was crystallized with Et_2O/PE to afford **14a** as a white crystalline solid: mp 46–48 °C; ^{1}H NMR δ 5.96 (s, 4 H), 3.26, 3.25 (overlapping s, 6 H), 2.3–1.6 (m, 6 H); IR (NaCl, cm^{-1}) 3400, 3300, 2940, 2110 (w), 1510, 1405, 1110, 1070–1030, 955; HRMS calcd for $C_{12}H_{16}O_3$ m/e 208.1100, obsd 208.1077.

4-(3-Butynyl)-4-hydroxycyclohexa-2,5-dienone (15a). HOAc (25 mL, 8% aqueous) was added to a solution of **14a** (160 mg, 0.77 mmol) in acetone (50 mL), and this solution was stored at 0 °C for 12 h, then saturated $NaHCO_3$ (25 mL) was added. Extractive workup with CH_2Cl_2 (3 × 25 mL) gave **15a** (108 mg, 86%) as a light brown oil that was >95% pure by ^{1}H NMR spectroscopy. A small sample was recrystallized using Et_2O/hexane and was sublimed to give **15a** as a white crystalline solid: mp 59–61 °C; ^{1}H NMR δ 6.50 (AB q, $\Delta\nu$ = 52 Hz, J = 10.2 Hz, 4 H), 2.3–1.9 (m, 5 H); IR (NaCl, cm^{-1}) 3380, 3300, 2110 (w), 1670, 1620, 1072, 1050, 860. Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.06; H, 6.21. Found: C, 74.00; H, 6.28.

2-Methylene-1-oxaspiro[4.5]deca-6,9-dien-8-one (16a). To a solution of **15a** (1.12 g, 6.9 mmol) in benzene (5 mL) and Et_3N (0.6 mL) was added $HgCl_2$ (300 mg, 1.1 mmol). The resulting suspension was stirred and heated at reflux for about 2 h. TLC analysis (60:40 Et_2O/PE) showed mostly vinyl ether **16a**, some isomerized vinyl ether **17a**, and some starting material. The suspension was cooled to rt, and the product was immediately chromtographed on flash silica gel (20 g) that had been previously washed with a 50:50 Et_3N/Et_2O mixture (200 mL) using 15% Et_2O/PE (2% Et_3N) as eluant. There was first obtained the endocyclic vinyl ether **17a** (56 mg, 5%) as a clear oil: ^{1}H NMR δ 6.46 (AB q, $\Delta\nu$ = 60 Hz, J = 10.1 Hz, 4 H), 4.65–4.58 (str m, 1 H), 2.75–2.64 (str m, 2 H), 1.81–1.74 (str m, 3 H); IR (NaCl, cm^{-1}) 1670, 1630, 1380, 1240, 1180, 950, 920, 850; HRMS calcd for $C_{10}H_{10}O_2$ m/e 162.0681, obsd 162.0699.

(12) **General Procedures.** Melting points were determined in capillaries and are uncorrected. Only strong absorptions are reported for IR spectra unless otherwise noted. ^{1}H NMR spectra were measured at 80 or 200 MHz in $CDCl_3$. Unless noted otherwise, reported spectra were at 80 MHz. All reagents or compounds not explicitly referenced were obtained from the Aldrich Chemical Co. Aluminum and silica gel (Kieselgel 60 230–400 mesh) were obtained from E. Merck Co. TLC was done using Merck silica gel 60 F_{254} precoated aluminum backed plates, 0.2-mm thick. All organometallic reactions were done under N_2 or Ar. Visualization was by UV or by spraying with 5% ethanolic phosphomolybdic acid and then heating. THF was purified by distillation from benzophenone ketyl. Throughout the Experimental Section the following abbrevations are used: petroleum ether, bp 35–60 °C (PE), *p*-toluenesulfonic acid (*p*-TsOH). Extractive workup refers to extraction of the material into the indicated solvent, washing the organic layer with brine solution, drying over Drierite ($CaSO_4$), concentration in vacuo, and drying to constant weight under vacuum (1–2 Torr). All quinone monoketals were handled in glassware washed with 5% NH_4OH.

(13) Belleau, B.; Weinberg, N. L. *J. Am. Chem. Soc.* **1963**, *85*, 2526.

(14) Nilisson, A.; Ronlán, A. *Tetrahedron Lett.* **1975**, 1107.

Continued elution gave the vinyl ether **16a** (470 mg, 42%) as a white crystalline solid: mp 71–73 °C; ^{1}H NMR δ 6.38 (AB q, $\Delta\nu$ = 33 Hz, J = 10 Hz, 4 H), 4.3 (m, 1 H), 3.95 (m, 1 H), 2.79 (t, J = 9 Hz, 2 H), 2.02 (t, J = 9 Hz, 2 H); IR (KBr, cm^{-1}) 1674, 1630, 1193, 1018; HRMS calcd for $C_{10}H_{10}O_2$ m/e 162.0681, obsd 162.0686.

Later in these studies the following improved procedure was employed for the preparation of **16a**. To a mixture containing $HgCl_2$ (179 mg, 1.06 equiv), benzene (15 mL), succinimide (62 mg, 1.06 equiv), and Et_3N (0.5 mL, 5.5 equiv) was added *p*-quinol **15a** (100 mg, 0.62 mmol). The resulting mixture was heated at 60 °C under N_2 for 5 min. At this time, TLC analysis of the slightly yellow homogeneous solution showed no starting material, a trace of isomerized vinyl ether, and **16a**. The mixture was filtered through Florisil (5 g) using 15% Et_2O/hexane as eluant to give **16a** (65 mg, 65%) as a white crystalline solid, identical with that obtained above.

Spiro[4.5]deca-6,9-diene-2,8-dione (18a). A solution of **16a** (0.410 g, 2.5 mmol) in benzene (10 mL) was placed in a screw-topped thick-walled tube. N_2 was bubbled through the solution for about 5 min, the top was attached, and the tube was heated at 150 °C for 22 h. After heating, a brown deposit of negligible weight, which was insoluble in several organic solvents, formed in the tube. The slightly yellow benzene solution was concentrated in vacuo, and the resulting brown oil was chromatographed on flash silica gel (230–400 mesh, 7 g) using $CHCl_3$ as eluant to give the diketone **18a** (0.315 g, 77%) as white crystals: mp 72–74 °C (lit.[15] mp 72–74 °C); ^{1}H NMR δ 6.56 (AB q, $\Delta\nu$ = 49 Hz, J = 10 Hz, 4 H), 2.8–2.5 (m, 2 H), 2.38 (s, 2 H), 2.3–2.0 (m, 2 H); IR (KBr, cm^{-1}) 1750, 1660, 1623, 860.

4-(1-Pentynyl)-4-hydroxycyclohexa-2,5-dienone Dimethyl Acetal (13b). The procedure was essentially that of **13a** using 1-pentyne (6 mL, 0.061 mol), CH_3Li (40 mL × 1.5 M, 0.060 mol), Et_2O (50 mL) at 0 °C, and **12** (5.2 g, 0.034 mol) to give **13b** (6.7 g, 89%) as a brown oil that was >95% pure by ^{1}H NMR spectroscopy; a small amount of unreacted **12** remained. This material was used in the subsequent chemistry. A purified sample was prepared by reaction of crude **13b** (1 g, 4.5 mmol) in CH_3OH (50 mL) at 0 °C with $NaBH_4$ (0.15 g). After 0.5 h, the CH_3OH was removed in vacuo, and the residue was treated with 5% NaOH (100 mL). Extractive workup with Et_2O (2 × 100 mL) gave pure **13b** (0.78 g, 78%) as a slightly yellow oil: ^{1}H NMR δ 6.07 (d, J = 10 Hz, 2 H), 5.68 (d, J = 10 Hz, 2 H), 3.12, 3.10 (overlapping s, 6 H), 2.2–2.0 (t, J = 6 Hz, 2 H), 1.7–1.2 (sextet, J = 6 Hz, 2 H), 1.0–0.7 (t, J = 6 Hz, 3 H); IR (NaCl, cm^{-1}) 3400, 2960, 2940, 2220 (w), 1460, 1410, 1210, 1150, 1105, 1060, 1040, 955; HRMS calcd for $C_{13}H_{18}O_3$ m/e 222.1256, obsd 222.1259.

4-(4-Pentynyl)-4-hydroxycyclohexa-2,5-dienone Dimethyl Acetal (14b). The terminal acetylene **14b** was prepared via the KAPA isomerization as described for **14a** using KH (15 g, 35% by wt, 0.13 mol), 1,3-diaminopropane (50 mL), and **13b** (5.4 g, 0.024 mol) in 1,3-diaminopropane (20 mL) to give **14b** (3.74 g, 69%) as a reddish oil, 95% pure by ^{1}H NMR spectroscopy. This material was used without further purification in subsequent chemistry. A sample of purified material was obtained by filtering the compound (75 mg) through a plug of activity III basic alumina (3 × 0.25 cm column, 5:45:50 Et_3N/hexane/Et_2O as eluant). Spectroscopic data are from this purified material: ^{1}H NMR δ 5.96 (AB q, $\Delta\nu$ = 23 Hz, J = 10.5 Hz, 4 H), 3.29, 3.27 (overlapping s, 6 H), 2.21–2.16 (m, 2 H), 1.94–1.91 (m, 1 H), 1.77–1.71 (m, 2 H), 1.54–1.46 (m, 2 H); IR (NaCl, cm^{-1}) 3350 (br), 3280, 2800–2970, 2100 (w), 1455, 1405, 1205, 1100, 1065, 1030, 950; HRMS calcd for $C_{13}H_{18}O_3$ m/e 222.1256, obsd 222.1251.

4-(4-Pentynyl)-4-hydroxycyclohexa-2,5-dienone (15b). The procedure is essentially that described for **15a** using HOAc (15 mL, 8%) and **14b** (3.54 g, 0.016 mol) in acetone (30 mL). Extractive workup with CH_2Cl_2 (3 × 50 mL) gave **15b** (2.2 g, 84%) as a reddish oil that crystallized to a yellow solid that was >95% pure by ^{1}H NMR spectroscopy. This material was used for subsequent chemistry, but a small sample was recrystallized (Et_2O/hexane) and sublimed [45 °C (1 Torr), 24 h] to give a white crystalline compound: mp 53–54 °C; ^{1}H NMR δ 6.47 (AB q, $\Delta\nu$ = 53 Hz, J = 10.2 Hz, 4 H), 3.6 (s, 1 H), 2.31–2.02 (m, 2 H), 1.99–1.61 (m, 3 H), 1.67–1.24 (m, 2 H); IR (NaCl, cm^{-1}) 3350 (br s), 3290, 2100 (w), 1670, 1625, 1020, 860; HRMS calcd for $C_{11}H_{12}O_2$ m/e 176.0837, obsd 176.0864. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.06; H, 6.21. Found: C, 74.00, H, 6.28.

2-Methylene-1-oxaspiro[5.5]undeca-7,10-dien-9-one (16b). To a solution of **15b** (251 mg, 15.2 mmol) in CH_2Cl_2 (10 mL) and Et_3N (0.5 mL) was added $HgCl_2$ (206 mg, 0.76 mmol). The precipitated mercury acetylide was filtered and dried in vacuo before use. To a solution of **15b** (400 mg, 2.4 mmol) in benzene (5 mL) were added Et_3N (0.2 mL, 3.6 equiv) and the mercury acetylide (400 mg, 0.76 mmol). The resulting slurry was heated at reflux for 4 h, after which time some cyclization had occurred, as well as some isomerization of the resulting vinyl ether. The solution was chromatographed through activity III neutral alumina (10 × 1 cm column, 5:10:85 Et_3N/Et_2O/hexane as eluant) to give three major products: starting material (210 mg, 52%), the exocyclic vinyl ether **16b** (70 mg, 18%, 37% based on recovered starting material), and isomerized vinyl ether **17b** (20 mg, 5%, 13% based on recovered starting material). The starting material was obtained as a red oil that crystallized upon addition of a seed crystal. The vinyl ethers were obtained as clear oils and are characterized as follows.

Exocyclic vinyl ether **16b**: ^{1}H NMR δ 6.96 (d, J = 10 Hz, 2 H), 6.09 (d, J = 10 Hz, 2 H), 4.35 (s, 1 H), 4.21 (s, 1 H), 2.23–2.21 (m, 2 H), 1.80–1.60 (m, 4 H); IR (NaCl, cm^{-1}) 1675, 1635, 1245, 1060, 1020; HRMS calcd for $C_{11}H_{12}O_2$ m/e 176.0837, obsd 176.0809.

Endocyclic vinyl ether **17b**: ^{1}H NMR δ 6.56 (AB q, $\Delta\nu$ = 64 Hz, J = 10.2 Hz, 4 H), 4.66 (m, 1 H), 2.3–1.9 (m, 2 H), 1.9–1.6 (m, 5 H); IR (NaCl, cm^{-1}) 2920, 2830, 1675, 1635, 1390, 1380, 1335, 1300, 1230, 1150, 1085, 1070, 1055, 1025, 995, 930, 870, 840; HRMS calcd for $C_{11}H_{12}O_2$ m/e 176.0837, obsd 176.0809.

Spiro[5.5]undeca-7,10-diene-2,9-dione (18b). A degassed solution of the vinyl ether **16b** (70 mg, 0.42 mmol) in benzene (2 mL) was heated in a sealed tube at 130 °C for 12 h. At the end of the reaction there was a clear solution with a small amount of a white precipitate (due to polymerization of a small amount of the endocyclic vinyl ether **17b** as an impurity) of negligible weight. This solution was filtered through a small column of silica gel (230–400 mesh, 10 × 0.5 cm column, $CHCl_3$ as eluant) to yield the spirodienedione (52 mg, 74%) as a clear oil that crystallized. Recrystallization from Et_2O/hexane gave **18b** as a white crystalline compound: mp 98–99 °C (lit.[15a] mp unreported); ^{1}H NMR δ 6.87 (d, J = 10 Hz, 2 H), 6.28 (d, J = 10 Hz, 2 H), 2.52–2.48 (t, J = 6.5 Hz, 2 H), 2.39 (s, 2 H), 2.17–2.09 (q, J = 6.5 Hz, 2 H), 1.92–1.88 (t, J = 6.5 Hz, 2 H); IR (KBr, cm^{-1}) 1700, 1665, 1630, 1410, 855; HRMS calcd for $C_{11}H_{12}O_2$ m/e 176.0838, obsd 176.0859.

4-(3-Butynyl)-4-hydroxycyclohexa-2,5-dienone Ethylene Acetal (19). To a solution of *p*-quinol ketal **14a** (1.5 g, 6.76 mmol) in ethylene glycol (100 mL) was added glacial HOAc (1 mL). The solution was stored at rt for 16 h, after which time the solution was poured into saturated aqueous $NaHCO_3$ (200 mL). Extractive workup with CH_2Cl_2 (3 × 100 mL) gave a colored solid. Addition of a small portion of Et_2O dissolved most of the impurities, and the resulting tan solid was collected by filtration to afford **19** (1.3 g, 88%, >95% pure by ^{1}H NMR spectroscopy). Recrystallization from Et_2O/hexane gave a white solid: mp 134–135 °C; ^{1}H NMR δ 5.94 (AB q, $\Delta\nu$ = 16 Hz, J = 10.3 Hz, 4 H), 4.02 (s, 4 H), 2.6–1.8 (m, 5 H); IR (KBr, cm^{-1}) 3410, 3280, 1420, 1110, 950; HRMS calcd for $C_{12}H_{14}O_3$ m/e 206.0943, obsd 206.0957.

4-(3-Pentynyl)-4-hydroxycyclohexa-2,5-dienone (20). To a rt solution of *p*-quinol ketal **19** (0.13 g, 0.63 mmol) in THF (10 mL) under Ar was added CH_3Li (1 mL × 1.5 M, 2.3 equiv). After 10 min, CH_3I (0.05 mL, 1.3 equiv) was added, and the resulting solution was stirred for 20 h. After the reaction mixture was poured into saturated aqueous $NaHCO_3$ (30 mL), extractive workup with CH_2Cl_2 (3 × 30 mL) gave the methylated acetylene (0.117 g, 84%) as a white crystalline material: mp 65–67 °C; ^{1}H NMR δ 5.89 (AB q, $\Delta\nu$ = 17 Hz, J = 10.3 Hz, 4 H), 4.05 (s, 4 H), 2.05–1.73 (m, 8 H); IR (KBr, cm^{-1}) 3440, 1415, 1110, 1010, 960, 940; HRMS calcd for $C_{13}H_{16}O_3$ m/e 220.1099, obsd 220.1128.

To a solution of the above compound (68 mg, 0.31 mmol) in acetone (10 mL) was added 2% aqueous HCl (10 mL). After 45

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min, the mixture was poured into saturated aqueous $NaHCO_3$ (30 mL). Extractive workup with CH_2Cl_2 (3 × 30 mL) gave a crude brown oil. Chromatography of this material on silica gel (230–400 mesh, 24 × $^1/_4$ cm column, 25% Et_2O/hexane as eluant) afforded the quinol (40 mg, 73%) as a slightly yellow oil: ^1H NMR (300 MHz) 6.86 (d, J = 10 Hz, 2 H), 6.15 (d, J = 10 Hz, 2 H), 2.79 (s, 1 H), 2.18 (m, 2 H), 1.93 (t, J = 7 Hz, 2 H), 1.73 (s, 3 H); IR (NaCl, cm^{-1}) 3350 (br s), 1670, 1625, 1080, 1050, 860; HRMS calcd for $C_{11}H_{12}O_2$ m/e 176.0837, obsd 176.0857.

1-Methylspiro[4.5]deca-6,9-diene-2,8-dione (21). A mixture containing **20** (0.2 g, 1.23 mmol) and $HgCl_2$ (335 mg, 1 equiv) in xylene (10 mL) was degassed and placed under Ar. Et_3N (1.05 mL, 6 equiv) was added, and the flask was heated to 140 °C. After 4 h, the reaction was shown to be complete by TLC (Et_2O). The reaction mixture was filtered through Florisil to give the diketone **21** (80 mg, 44%) as a brown oil, ca. 95% pure by ^1H NMR spectroscopy. Careful chromatography through silica gel (230–400 mesh, 24 × 0.5 cm column, 1:2 Et_2O/hexane as eluant) afforded the diketone **21** (70 mg, 35%) as a white crystalline solid, mp 83–85 °C. Recrystallization from Et_2O/hexane afforded the analytically pure material: mp 91–92 °C (lit.[15d] mp 93–94 °C); ^1H NMR (300 MHz) δ 6.84–6.80 (m, 1 H), 6.67–6.62 (m, 1 H), 6.42–6.35 (m, 2 H), 2.67–2.41 (m, 3 H), 2.40–2.02, (m, 2 H), 0.86 (d, J = 7 Hz, 3 H); IR (KBr, cm^{-1}) 1745, 1660, 860.

1-Phenylspiro[4.5]deca-6,9-diene-2,8-dione (24). A solution of iodobenzene (117 mg, 0.57 mmol), CuI (5 mg, 5%), and $PdCl_2(PPh_3)_2$ (17 mg, 5%) in diisopropylamine (5 mL) was degassed and placed under Ar. A solution of **14a** (100 mg, 0.48 mmol) in diisopropylamine (2 mL) was added dropwise. After 3 h a precipitate formed and was filtered off. The filtrate was concentrated, and the resulting red oil was chromatographed through neutral alumina (activity III, 24 × $^1/_4$ cm column, 25–50% Et_2O/hexane as eluant) to give the phenyl acetylene derivative (91 mg, 67%) as an oil: ^1H NMR δ 7.45–7.20 (m, 5 H), 6.18–5.86 (br s, 4 H), 3.30, 3.28 (overlapping s, 6 H), 2.62–2.29 (m, 3 H), 2.07–1.85 (m, 2 H); IR (NaCl, cm^{-1}) 3400, 2940, 1490, 1445, 1410, 1110, 1070, 950, 910, 760, 740, 690; HRMS calcd for $C_{18}H_{20}O_3$ m/e 284.1412, obsd 284.1430.

A solution of the phenylacetylene from above (100 mg, 0.35 mmol), 18-crown-6 (23 mg), and KOH (23 mg) in THF (5 mL) was heated at reflux under N_2 for 2 h. Filtration of the resulting brown solution through Florisil (24 × $^1/_4$ cm column, 25% Et_2O/PE as eluant) afforded a cis, trans mixture of vinyl ethers (96 mg of a crude yellow oil). Hydrolysis of the ketal was effected by dissolving the compound in acetone/8% aqueous HOAc (3 mL:1.5 mL). After 7 min, the mixture was poured into saturated aqueous $NaHCO_3$ (15 mL). Extractive workup gave the crude hydrolysis product as a crude yellow oil (70 mg). Chromatography of this material on silica gel (230–400 mesh, 24 × $^1/_4$ cm column, 25% Et_2O/PE as eluant) afforded **23** (51 mg, 61%) as a slightly yellow solid. High-field NMR spectroscopy showed the compound to be a 3:2 mixture of cis,trans isomers. The melting point of this solid was unattainable since thermal rearrangement was observed in the melting point capillary tube, as verified by IR spectroscopy.

A solution of **23** (70 mg) from above in benzene (1 mL) was degassed and heated at 80 °C for 16 h. Chromatography through silica gel (4 × $^1/_4$ cm column, 35% Et_2O/PE as eluant) afforded **24** (50 mg, 71%) as a white crystalline solid, mp 135–138 °C. Recrystallization from Et_2O/PE raised the melting point to 141–143 °C. This material showed: ^1H NMR (300 MHz) δ 7.25–7.20 (m, 2 H), 7.05–6.9 (m, 3 H), 6.85 (dd, J = 3, 10 Hz, 1 H), 6.36 (d, J = 10 Hz, 1 H), 6.13 (d, J = 10 Hz, 1 H), 3.7 (s, 1 H), 2.8–2.65 (m, 2 H), 2.4–2.3 (m, 1 H), 2.25–2.1 (m, 1 H); IR (KBr, cm^{-1}) 1745, 1660, 1625, 1405, 1140, 870, 750, 700; HRMS calcd for $C_{16}H_{14}O_2$ m/e 238.0993, obsd 238.0986.

10-(Phenylmethylene)-1,4,9-trioxadispiro[4.2.4.2]tetradeca-6,13-diene (25). A solution of iodobenzene (88 mg, 0.42 mmol), CuI (4 mg, 5%), and $PdCl_2(PPh_3)_2$ (13 mg, 5%) in diisopropylamine (5 mL) was degassed and placed under Ar. A solution of **19** (78 mg, 0.38 mmol) in diisopropylamine (5 mL) was added dropwise.[16] After 3 h, the solution was a heterogeneous dark brown. The precipitate was removed by filtration through Celite, and the solvent was removed in vacuo to yield a red oil. Filtration through silica gel (230–400 mesh, 12.4 × 0.25 cm column, 25% Et_2O/PE as eluant) afforded the phenyl acetylene (74 mg, 69%) as a white crystalline solid, mp 120–122 °C. Recrystallization from Et_2O/hexane raised the melting point to 122–123 °C. This material showed: ^1H NMR δ 7.38–7.18 (m, 5 H), 5.92 (AB q, $\Delta\nu$ = 18 Hz, J = 10 Hz, 4 H), 4.03 (s, 4 H), 2.49–2.26 (m, 2 H), 2.06–1.85 (m, 2 H), 1.83 (s, 1 H); IR (KBr, cm^{-1}) 3400, 1420, 1110, 1080, 850, 750; HRMS calcd for $C_{18}H_{18}O_3$ m/e 282.1255, obsd 282.1246.

A solution of the phenyl acetylene from above (30 mg, 0.106 mmol), KOH (15 mg), and 18-crown-6 (15 mg) in THF (5 mL) was heated at reflux under N_2 for 2 h. Concentration and chromatography of the product through silica gel (230–400 mesh, 24 × $^1/_4$ cm column, 15% Et_2O/hexane as eluant) gave **25** (26 mg, 87%) as a white crystalline solid: mp 85–87 °C; ^1H NMR δ 7.56–6.6 (m, 2 H), 7.48–7.03 (m, 3 H), 6.02 (AB q, $\Delta\nu$ = 22 Hz, J_{AB} = 10 Hz, 4 H), 5.25 (s, 1 H), 4.09 (s, 4 H), 3.00–2.81 (t, J = 8 Hz, 2 H), 2.13–1.93 (t, J = 8 Hz, 2 H); IR (KBr, cm^{-1}) 1670, 1415, 1370, 1160, 1110, 1060, 1010, 960, 760, 690; HRMS calcd for $C_{18}H_{18}O_3$ m/e 282.1255, obsd 282.1289.

9-Phenyl-1,3-dioxadispiro[4.2.4.2]tetradeca-6,13-dien-10-one (26). A solution of **25** (45 mg, 0.16 mmol) was dissolved in benzene (1 mL) and degassed by bubbling N_2 through the solution for 5 min. The solution was irradiated through Pyrex using RPR-3000 Å lamps for 12 h. Concentration and chromatography through silica gel (230–400 mesh, 24 × $^1/_4$ cm column, 25% Et_2O/PE as eluant) afforded **26** (25 mg, 56%) as a white crystalline solid: mp 125–127 °C; ^1H NMR (300 MHz) δ 7.3–7.2 (m, 3 H), 7.0–6.9 (m, 2 H), 6.16 (d, J = 10 Hz, 1 H), 5.92 (d, J = 10 Hz, 1 H) 5.83 (d, J = 10 Hz, 1 H), 5.62 (d, J = 10 Hz, 1 H), 4.0–3.85 (m, 4 H), 3.5 (s, 1 H), 2.7–2.55 (m, 2 H), 2.25–2.05 (m, 2 H); IR (KBr, cm^{-1}) 1730, 1100, 950, 700; HRMS calcd for $C_{18}H_{18}O_3$ m/e 282.1255, obsd 282.1255.

4-(2-Hydroxyethoxy)-4-phenylcyclohexa-2,5-dienone (28). Iodobenzene diacetate (2.1 g, 6.4 mmol) was added in 0.5-g portions every 10–15 min to a suspension of p-phenylphenol (1.0 g, 5.9 mmol) in ethylene glycol (40 mL). After a total reaction time of 2 h, TLC (30% EtOAc/hexane) analysis showed no sign of starting material, and the reaction mixture was poured into water (30 mL). Extractive workup with CH_2Cl_2 (3 × 75 mL) gave a dark purple liquid (3.0 g). The crude product was chromatographed on Florisil [2.5 × 12 cm column; hexane (50 mL), 20% EtOAc/hexane (50 mL), 40% EtOAc/hexane (300 mL) as eluant] to give the dienone as a yellow solid (1.05 g, 77%). The pure product was obtained as a white solid by recrystallization from EtOAc/hexane: mp 79–80 °C; IR (KBr, cm^{-1}) 3320 (br), 1665, 1053; ^1H NMR (200 MHz) δ 7.5–7.3 (m, 5 H), 6.82 (d, J = 10.1, Hz, 2 H), 6.37 (d, J = 10.1 Hz, 2 H), 3.9–3.75 (m, 2 H), 3.7–3.6 (m, 2 H), 2.01 (t, J = 5.7 Hz, 1 H). Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.39; H, 6.32.

4-Phenyl-4-hydroxycyclohexa-2,5-dienone Ethylene Acetal. To a solution of benzoquinone monoethylene ketal[5a] (5.0 g, 33 mmol) in THF (40 mL) at −78 °C was added PhLi (23 mL of a 1.69 M solution, 39 mmol) using a syringe pump (0.65 mL/min). The reaction mixture was stirred at −78 °C for 1.5 h, then warmed to rt, stirred an additional 3 h, and then poured into H_2O (100 mL). Extractive workup with Et_2O (3 × 75 mL) yielded a yellow-orange solid (7.3 g, 96%), mp 115–119 °C. Recrystallization from Et_2O gave the quinol as a white crystalline solid: mp 129–130 °C; IR (KBr, cm^{-1}) 3405, 1110, 945; ^1H NMR (200 MHz) δ 7.5–7.25 (m, 5 H), 5.95 (AB q, $\Delta\nu$ = 35 Hz, J = 10 Hz, 4 H), 4.1 (s, 4 H), 2.26 (s, 1 H). Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.47; H, 6.22.

4-Phenyl-4-(allyloxy)cyclohexa-2,5-dienone Ethylene Acetal (9b). A solution of the above alcohol (2.0 g, 8.7 mmol) in THF (10 mL) was added dropwise via syringe to a suspension of NaH (0.38 g of a 60% mineral oil dispersion, 9.6 mmol) in THF (5 mL), and the resulting solution was stirred at rt for 30 min. Allyl bromide (1.1 mL, 13 mmol) was then added via syringe, and the reaction mixture was heated at 50 °C for 30 h. After addition of H_2O (15 mL), extractive workup with Et_2O (3 × 30 mL) gave 2.28 g (97%) of a light yellow solid (mp 41–44 °C). Recrystallization from Et_2O/hexane gave the pure allyl ether: mp 47–48 °C; IR (KBr, cm^{-1}) 1410, 1110, 1055, 1010, 960, 945, 753, 695; ^1H NMR (250 MHz) δ 7.49 (d, J = 8.5 Hz, 2 H), 7.35–7.15 (m, 3 H), 6.1–5.9 (m, 5 H), 5.4–5.3 (m, 1 H), 5.2–5.1 (m, 1 H), 4.09 (s, 4 H),

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4.05–3.95 (m, 2 H). Anal. Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.45; H, 6.68.

4-Phenyl-4-(allyloxy)cyclohexa-2,5-dienone (29). A solution of 2% HCl (10 mL) was added to a solution of **9b** (1.1 g, 4.1 mmol) in THF (15 mL) at 0 °C. The resulting solution was stirred at 0 °C for 5 h and was then poured into saturated $NaHCO_3$ (40 mL). Extractive workup with Et_2O (3 × 40 mL) gave a light yellow oil (0.96 g). Chromatography on silica gel [15 × 2 cm column; 5% Et_2O/hexane (20 mL), 10% Et_2O/hexane (100 mL) as eluant] gave the dienone **29** (0.91 g, 98%) as a white solid (mp 41–45 °C). Recrystallization of a portion of this solid from hexane yielded pure **29**: mp 43–44 °C; IR (KBr, cm^{-1}) 1670, 1628, 690; ^1H NMR (200 MHz) δ 7.5–7.3 (m, 5 H), 6.59 (AB q, $\Delta\nu$ = 83 Hz, J = 10.2 Hz, 4 H), 6.05–5.9 (m, 1 H), 5.4–5.15 (m, 2 H), 4.1–4.05 (m, 2 H). Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.89; H, 6.31.

$[(C_8H_{12})Ir(PMePh_2)_2]PF_6$.[17] To a suspension of cyclooctadiene chloroiridium dimer, $[(C_8H_{12})IrCl]_2$ (0.32 g, 1.0 mmol, Alpha Chemical Company), in EtOH (16 mL) was added $CH_3(Ph)_2P$ (0.56 mL, 3.0 mmol) dropwise via syringe under an Ar atmosphere. The solution immediately turned from orange-red to very dark red, and this solution was stirred at rt until it became homogeneous (15 min). A solution of NH_4PF_6 (1.0 g, 6.0 mmol) in EtOH (12 mL) was then added dropwise via syringe. A precipitate formed immediately, and the resulting orange-red mixture was cooled to 0 °C and stirred for 30 min. The product was then vacuum filtered, washed with cold EtOH and then Et_2O, and dried to yield a light pink solid (0.844 g, 96%); mp 170–175 °C (lit.[17] 236 °C dec). *Note: three different samples of this catalyst showed three different melting points: the one prepared above, a second preparation (mp 190–193 °C), and a commercial sample from Aldrich (mp 205–210 °C).* None of these catalysts gave a melting point corresponding to the literature value, yet all three batches effected the isomerization.

***cis*- and *trans*-2-Hydroxy-3-methyl-5-phenyldihydrobenzofuran (32, 33).** A suspension of $[(COD)Ir(PPh_2Me)_2]PF_6$ (0.015 g, 0.02 mmol) in THF was activated with H_2 as for **40**, then allyl ether **29** (0.05 g, 0.2 mmol) was added via syringe as a solution in THF (2 mL). The resulting solution was stirred at rt for 12 h, and the solvent was removed under vacuum. The crude product was chromatographed on Florisil [2 × 15 cm column; 10% Et_2O/hexane (150 mL) as eluant] to give the colorless liquid dihydrobenzofurans **32** and **33** (0.04 g, 80%) as a mixture of diastereomers: IR (melt, cm^{-1}) 3380 (br), 1470, 755; ^1H NMR see supplementary material; HRMS calcd for $C_{15}H_{14}O_2$ m/e 226.0993, obsd 226.0982.

3-Methyl-5-phenylbenzofuran (34). *p*-Toluenesulfonic acid (5 mg) was added to a solution of **32**, **33** (0.04 g, 0.18 mmol) in benzene (10 mL), and the resulting solution was heated at reflux for 5 h. The cooled reaction mixture was diluted with H_2O (15 mL) and, after extractive workup with Et_2O (2 × 10 mL), gave a yellow oil (0.034 g). Chromatography on flash silica gel [1 × 15 cm column; hexane (50 mL) as eluant] afforded **34** as a white solid, 0.03 g (81%): mp 57–59 °C; IR (KBr, cm^{-1}) 1460, 1445, 1080, 750; ^1H NMR (500 MHz) δ 7.7 (s, 1 H), 7.63 (dd, J = 1, 8 Hz, 2 H), 7.52–7.42 (m, 5 H), 7.35–7.3 (m, 1 H), 2.28 (d, J = 1.2 Hz, 3 H); HRMS calcd for $C_{15}H_{12}O$ m/e 208.0888, obsd 208.0848.

1-(2-Hydroxyethoxy)-2-(1-oxopropyl)biphenyl (36). The procedure was essentially the same as that employed for the preparation of **40** using $[(COD)Ir(PPh_2Me)_2]PF_6$ (0.01 g, 0.012 mmol, 1.5 mol %) in THF (3 mL) and the allyl ether **9b** (0.20 g, 0.75 mmol) in THF (2 mL). After 1.5 h reaction workup gave a thick yellow oil (0.21 g). The crude product was chromatographed on Florisil [1 × 10 cm column; 10% EtOAc/hexane (20 mL), 20% EtOAc/hexane (20 mL), 40% EtOAc/hexane (25 mL) as eluant] to give a colorless oil (0.16 g, 75%). The initial product was not analytically pure, but spectral data indicated that it was the cyclohexadiene **35**: IR (melt, cm^{-1}) 1725; ^1H NMR (200 MHz) δ 9.64 (d, J = 2.2 Hz, 1 H), 7.45–7.2 (m, 5 H), 6.47 (dd, J = 2, 9.9 Hz, 1 H), 6.05–6.0 (m, 1 H), 5.85 (d, J = 10 Hz, 1 H), 4.1–3.85 (m, 4 H), 3.26 (dd, J = 4.5, 6.8 Hz, 1 H), 2.9–2.7 (str m, 1 H), 1.19 (d, J = 7.2 Hz, 3 H). This product was converted to **36** by heating a solution of the cyclohexadiene in CH_2Cl_2 on a steam bath for 2 h: ^1H NMR (200 MHz) δ 9.68 (d, J = 1.1 Hz, 1 H), 7.6–7.3 (m, 7 H), 6.94 (d, J = 8.6 Hz, 1 H), 4.1–3.9 (m, 4 H), 3.79 (q, J = 7.2 Hz, 1 H), 2.3 (br s, 1 H), 1.45 (d, J = 7.0 Hz, 3 H).

The aldehyde was found to decompose over a period of days, so it was converted to its 2,4-dinitrophenyl hydrazone (2,4-DNP). Recrystallization of this material from EtOH gave the pure 2,4-DNP: mp 169–170 °C; IR (KBr, cm^{-1}) 1615, 1585, 1510, 1330, 1305; ^1H NMR (200 MHz) δ 11.0 (s, 1 H), 9.08 (d, J = 2.5 Hz, 1 H), 8.30 (dd, J = 2.5, 9.6 Hz, 1 H), 7.92 (d, J = 9.6 Hz, 1 H), 7.69 (d, J = 5.5 Hz, 1 H), 7.5–7.3 (m, 7 H), 6.96 (d, J = 8.4 Hz, 1 H), 4.4–4.2 (m, 1 H), 4.15 (t, J = 4.3 Hz, 2 H), 4.05–3.95 (m, 2 H), 1.60 (d, J = 7.0 Hz, 3 H). Anal. Calcd for $C_{23}H_{22}N_4O_6$: C, 61.33; H, 4.92. Found: C, 61.11; H, 5.27.

1-Phenyl-1-(prop-1-enyloxy)cyclohexane (40). The iridium catalyst (0.015 g, 0.018 mmol) prepared above was activated by placing a suspension of the catalyst in THF (2 mL) under a H_2 atmosphere. A color change from red to light yellow along with formation of a homogeneous solution indicated that the catalyst had been activated. The reaction vessel was evacuated and back-filled with N_2 three times, and the allyl ether **39** (0.209 g, 0.97 mmol) was added as a solution in THF (3 mL) via syringe. After stirring at rt for 10 h, ^1H NMR analysis indicated the reaction was complete. The solvent was removed under vacuum, and the crude reaction mixture was chromatographed on a Florisil column (4 × 1 cm, 10% ether/hexane as eluant) to yield pure vinyl ether **40** (0.195 g, 93%): IR (melt, cm^{-1}) 2925, 2845, 1665, 1442, 1155, 1127, 910; ^1H NMR δ 7.5–7.15 (m, 5 H), 5.73 (dd, J = 12.1, 1.6 Hz, 1 H), 5.15–4.90 (m, 1 H), 2.15–1.2 (m, 10 H), 1.42 (dd, J = 6.8, 1.6, 3 H); HRMS calcd for $C_{15}H_{20}O$ m/e 216.1514, obsd 216.1466.

Dimethyl Titanocene.[18] CH_3Li (16.4 mL of a 1.22 M solution, 20.0 mmol) was added dropwise to a suspension of Cp_2TiCl_2 (2.0 g, 8.0 mmol, Alpha) in dry Et_2O (100 mL) under Ar at 0 °C. The reaction mixture turned from dark red to orange, and after stirring at 0 °C for 10 min, the solution was warmed to rt for another 20 min. **The following operations were performed as quickly as possible in a dark room.** The reaction was quenched by adding H_2O (50 mL), and the layers were separated. The organic phase was washed with H_2O (2 × 20 mL) and dried over Na_2SO_4. Removal of the solvent in vacuo gave an orange solid (1.4 g). Recrystallization from hexane gave dimethyltitanocene (1.2 g, 72%) as bright orange needles.

4-Acetoxy-4-phenylcyclohexa-2,5-dienone Ethylene Acetal (41). To a solution of the alcohol, 4-hydroxy-4-phenyl-2,5-cyclohexadienone ethylene ketal (0.50 g, 2.17 mmol), in CH_2Cl_2 (15 mL) were added Ac_2O (0.5 mL, 5.0 mmol), pyridine (0.75 mL), and DMAP (45 mg). After being stirred at rt for 2 days, the reaction mixture was poured into 5% $NaHCO_3$. The organic layer was washed with H_2O (15 mL), dried, and concentrated to yield a light brown oil (0.6 g) which was purified by chromatography on silica gel [2 × 20 cm column; 10% EtOAc/hexane (100 mL), 20% EtOAc/hexane (100 mL) as eluant]. The acetate **41** was obtained as a light yellow solid (0.5 g, 85%). Recrystallization from Et_2O/hexane gave pure **41**: mp 86–87 °C; IR (KBr, cm^{-1}) 1745, 1230, 1110, 968, 945; ^1H NMR (200 MHz) δ 7.5–7.2 (m, 5 H), 6.25 (d, J = 10.2 Hz, 2 H), 5.94 (d, J = 10.1 Hz, 2 H), 4.08 (s, 4 H), 2.09 (s, 3 H). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.65; H, 5.87.

1-(2-Hydroxyethoxy)-2-(2-methyl-2-propenyl)biphenyl (44). $Cp_2Ti(CH_3)_2$ (1.2 mL of a 0.486 M toluene solution, 0.6 mmol) was added via syringe to an Al foil wrapped flask containing the quinol acetate **41**, and the resulting solution was heated at 75 °C for 24 h under Ar. The cooled reaction mixture was diluted with hexane (5 mL), filtered, and chromatographed on flash silica gel [15 × 2 cm column; 10% EtOAc/hexane (300 mL) as eluant]. Compound **44** was obtained as a white solid (0.34 g, 53%): mp 52–54 °C; IR (melt, cm^{-1}) 3400 (br), 1485, 1240, 750; ^1H NMR (200 MHz) 7.6–7.2 (m, 7 H), 6.89 (d, J = 8.3 Hz, 1 H), 4.8 (br s, 1 H), 4.68 (br s, 1 H), 4.11 (t, J = 4.9 Hz, 2 H), 3.95–3.85 (m, 2 H), 3.40 (s, 2 H), 1.73 (s, 3 H); HRMS calcd for $C_{18}H_{20}O_2$ m/e 268.1463, obsd 268.1455.

Kinetics of Rearrangement of 16a. The kinetics of the vinyl ether rearrangement of **16a** were followed by measuring the

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concentration of **18a** by GC using thermal conductivity detection (24 in. × $^1/_4$ in. column of 5% OV-101 at 160 °C, and the peak areas were measured on a digital integrator. The samples for the kinetic determinations were prepared from a stock solution of approximately 0.05–0.1 M **16a** in benzene containing heptadecane as internal standard. These samples were degassed using three freeze–thaw cycles and sealed in glass ampoules. Appropriate calibration solutions were employed in the GC analysis. The kinetics were studied at two different concentrations with identical rate constants (within experimental error) being measured. The average rate constant obtained from three different runs was 1.5×10^{-4} s^{-1}. The maximum error in this value is estimated to be ±8%. Detailed procedures and a representative kinetic plot are given in the supplementary material.

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Registry No. **6**, 15791-03-4; **9b**, 135614-81-2; **12**, 935-50-2; **13a**, 135614-71-0; **13b**, 135639-18-8; **14a**, 135614-72-1; **14b**, 135614-65-2; **15a**, 135614-73-2; **15b**, 135614-66-3; **16a**, 135614-74-3; **16b**, 135614-67-4; **17a**, 135614-92-5; **17b**, 135639-20-2; **18a**, 52727-26-1; **18b**, 52727-32-9; **19**, 135639-21-3; **20**, 135614-75-4; **21**, 66629-00-3; (*E*)-**22**, 135614-70-9; (*Z*)-**22**, 135614-76-5; (*E*)-**23**, 135614-82-3; (*Z*)-**23**, 135614-77-6; **24**, 135639-22-4; **25**, 135614-78-7; **26**, 135614-79-8; **27**, 92-69-3; **28**, 135639-23-5; **29**, 135614-80-1; **32**, 135639-24-6; **33**, 135614-83-4; **34**, 135614-84-5; **35**, 135639-25-7; **36**, 135614-85-6; **36** 2,4-DNP hydrazone, 135614-68-5; **37**, 135614-86-7; **38**, 135614-87-8; **39**, 135614-88-9; **40**, 135614-89-0; **41**, 135614-90-3; **44**, 135614-91-4; $[(COD)Ir(PPh_2Me)_2]PF_6$, 38465-86-0; 4-hydroxy-4-phenylcyclohexa-2,5-dienone, 135639-19-9; ethylene acetal benzoquinone monoethylene ketal, 35357-34-7; 4-hydroxy-4-(4-phenyl-3-butynyl)cyclohexa-2,5-dienone dimethyl acetal, 135614-69-6; 1-butyne, 107-00-6; 1-pentyne, 627-19-0.

Supplementary Material Available: Experimental procedures for reactions of **9a**, **39**, **29**, **37**, and **38** and kinetic studies; NMR spectra of products (43 pages). Ordering information is given on any current masthead page.

Phase-Transfer Catalyzed Formation of α-Cyano Ketones from Ketone Aroylhydrazones in NaCN(aq)–Inert Organic Solvent System

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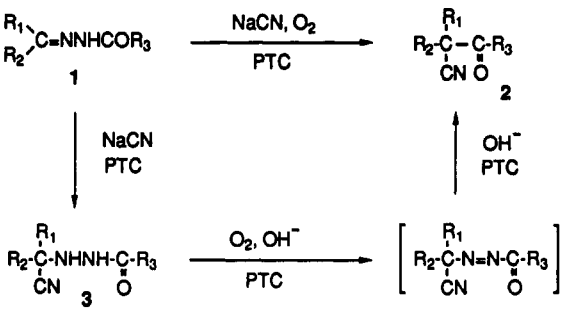
α-Cyanoalkyl aryl ketones can be obtained from ketone aroylhydrazones by heterogeneous reaction with aqueous sodium cyanide, an inert organic solvent, and acetic acid in the presence of air and a catalytic amount of a quaternary ammonium salt. The initially formed HCN adducts undergo air oxidation followed by alkaline-induced decomposition affording the α-cyanoalkyl ketones. The phase-transfer catalyst promotes all three reactions.

Previously, we reported the preparation of 1-(cyanoalkyl)-2-acylhydrazines from ketone hydrazones utilizing phase-transfer catalysis (PTC). These reactions were carried out in a stoppered flask in all cases.[1] Subsequently, it was found that the identical reaction run in an open flask in contact with air afforded α-cyanoalkyl aryl ketones (**2**). The cyano ketones were presumed to arise from the decomposition of the corresponding diazene generated by the oxidation of the HCN adduct (**3**). The formation of **2** from **1** involving carbon–carbon bond formation under mild conditions appears to be an attractive synthetic process.

The application of PTC for the oxidation of organic compounds has widely been investigated by using anionic oxidants such as permanganate, chromate, hypochlorite, periodate, or super oxide or by the combined use of metal catalysts;[2,3] however, examples of air oxidation promoted by quaternary ammonium salts seem to be limited.[4] Therefore, we have investigated phase-transfer catalysis of the present reaction and have applied the procedure to the synthesis of various α-cyanoalkyl aryl ketones **2** (Scheme I).

Scheme I



Results and Discussion

Addition of HCN to Ketohydrazones and Air Oxidation of the Resulting HCN Adducts. The reaction progress in the presence or absence of air was examined

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