H6(ax)), 3.72-3.58 (m, 2 H, H8, H8'), 3.35 (s, 3 H, O*Me*), 2.76 (d, 1 H, $J_{12,12'}$ = 17.3 Hz, H12), 2.61 (d, 1 H, $J_{12,12'}$ = 17.3 Hz, H12'), 2.09-1.97 (m, 1 H, H7), 1.77 (dd, 3 H, $J_{9,13}$ = 1.5 Hz, $J_{10,13}$ = 6.4 Hz, H13's), 1.59-1.48 (m, 1 H, H7'), 1.31 (s, 3 H, H14's), 0.88 (s, 9 H, Si^t*Bu*), 0.04 (s, 6 H, SiMe_2). Anal. Calcd for $C_{28}H_{43}NO_5Si$: C, 67.03; H, 8.64. Found: C, 66.87; H, 8.57.

Methyl 4,6-*O*-Benzylidene-3-*C*-(cyanomethyl)-2,3-dideoxy-2-*C*-(2-iodoethyl)-2-*C*-methyl-3-*C*-((*E*)-1-propenyl)-α-D-allopyranoside (38d). A mixture of nitrile **38c** (110 mg, 0.220 mmol) and tetrabutylammonium fluoride (0.24 mL, 1.0 M in THF, 0.242 mmol) in tetrahydrofuran (2 mL) was stirred at room temperature for 2 h, concentrated in vacuo, and passed through a short column of silica gel (60% EtOAc/petroleum ether) to give the alcohol as a colorless oil. To a mixture of the alcohol, triphenylphosphine (173 mg, 0.660 mmol), and imidazole (90 mg, 1.32 mmol) in benzene (2 mL) under argon was added iodine (168 mg, 0.660 mmol) in three portions. The reaction mixture was stirred at room temperature for 5 min, followed by addition of saturated aqueous sodium bisulfite (1 mL). After all solids had dissolved, ethyl acetate (10 mL) was added, and the organic layer was washed with saturated aqueous sodium bicarbonate solution (2 × 2 mL) and brine and then dried (Na_2SO_4). Evaporation of the solvent followed by flash chromatography (20% EtOAc/petroleum ether) gave **38d** (81 mg, 74%) as a clear glass: R_f 0.45 (1:1 CH_2Cl_2/10% EtOAc/petroleum ether); $[\alpha]^{19}_D$ +20.4° (*c* 1.95, $CHCl_3$); IR (neat) 2250 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.29 (m, 5 H, aromatic), 6.13 (d, 1 H, $J_{9,10}$ = 16.0 Hz, H9), 5.57-5.42 (m, 2 H, PhC*H*, H10), 4.33-4.23 (m, 2 H, H1, H6(eq)), 4.00 (ddd, 1 H, $J_{4,5}$ = 9.6 Hz, $J_{5,6(eq)}$ = 4.8 Hz, $J_{5,6(ax)}$ = 10.1 Hz, H5), 3.83 (d, 1 H, $J_{4,5}$ = 9.6 Hz, H4), 3.71 (dd, 1 H, $J_{5,6(ax)}$ = 10.1 Hz, $J_{6(eq),6(ax)}$ = 10.1 Hz, H6(ax)), 3.37 (s, 3 H, O*Me*), 3.21-3.10 (m, 1 H, H8), 3.05-2.94 (m, 1 H, H8'), 2.73 (d, 1 H, $J_{12,12'}$ = 17.2 Hz, H12), 2.62 (d, 1 H, $J_{12,12'}$ = 17.2 Hz, H12'), 2.44 (ddd, 1 H, $J_{7,7'}$ = 13.4 Hz, $J_{7,8}$ = 13.4 Hz, $J_{7,8'}$ = 4.9 Hz, H7), 1.96 (ddd, 1 H, $J_{7,7'}$ = 13.4 Hz, $J_{7',8}$ = 4.9 Hz, $J_{7',8'}$ = 13.4 Hz, H7), 1.80 (d, 3 H, $J_{10,13}$ = 6.4 Hz, H13's), 1.29 (s, 3 H, H14's); HRMS (CI/NH_3) 515.1407 (M + NH_4)$^+$, calcd for $C_{22}H_{32}N_2O_4I$ 515.1412.

(10*R*)-Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-2-*C*-methyl-α-D-glucopyranosido[3,2-*c*]-10-methylbicyclo-[3.3.0]octan-11-one (39).[13] Compound **38d** (55 mg, 0.11 mmol) was cyclized by the standard free-radical procedure over 1 h to give **39** (30 mg, 73%) as a white solid: mp 138-155 °C; R_f 0.35 (1:1 CH_2Cl_2/10% EtOAc/petroleum ether); $[\alpha]^{22}_D$ -5.2° (*c* 0.77, $CHCl_3$); IR (neat) 1740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (br s, 5 H, aromatic), 5.49 (s, 1 H, PhC*H*), 4.30 (dd, 1 H, $J_{5,6(eq)}$ = 5.0 Hz, $J_{6(eq),6(ax)}$ = 10.2 Hz, H6(eq)), 4.22 (s, 1 H, H1), 4.08 (ddd, 1 H, $J_{4,5}$ = 10.2 Hz, $J_{5,6(eq)}$ = 5.0 Hz, $J_{5,6(ax)}$ = 9.5 Hz, H5), 3.77 (d, 1 H, $J_{4,5}$ = 10.2 Hz, H4), 3.72 (dd, 1 H, $J_{5,6(ax)}$ = 9.5 Hz, $J_{6(eq),6(ax)}$ = 10.2 Hz, H6(ax)), 3.35 (s, 3 H, O*Me*), 3.29-3.18 (m, 1 H, H9), 2.95-2.84 (m, 1 H, H10), 2.29 (d, 1 H, $J_{12,12'}$ = 19.2 Hz, H12), 2.18 (d, 1 H, $J_{12,12'}$ = 19.2 Hz, H12'), 1.98-1.83 (m, 1 H, H8), 1.81-1.71 (m, 1 H, H7), 1.51-1.20 (m, 2 H, H7', H8'), 1.10 (s, 3 H, H14's), 0.97 (d, 3 H, $J_{10,13}$ = 7.1 Hz, H13's). Anal. Calcd for $C_{22}H_{28}O_5$: C, 70.94; H, 7.58. Found: C, 70.78; H, 7.82.

Registry No. **1**, 63598-31-2; **11**, 114129-69-0; **12**, 122674-58-2; (*E*)-**13**, 122592-03-4; (*Z*)-**13**, 122592-04-5; (*E*)-**14a**, 122592-05-6; (*Z*)-**14a**, 122592-06-7; (*E*)-**14b**, 122592-09-0; (*Z*)-**14b**, 122592-10-3; (*E*)-**15**, 122592-07-8; (*E*)-**15** aldehyde, 122592-26-1; (*Z*)-**15**, 122592-08-9; **16a**, 122592-11-4; **16b**, 122592-12-5; **16c**, 122592-13-6; **17**, 122592-14-7; **18**, 122672-65-5; **19**, 122672-66-6; **20**, 122592-15-8; **21**, 122592-16-9; **22a**, 122622-39-3; **22b**, 122592-17-0; **23a**, 122622-40-6; **23b**, 122622-17-7; **23c**, 122592-18-1; **24a**, 122592-19-2; **24b**, 122592-20-5; **25** isomer 1, 122592-21-6; **25** isomer 2, 122592-22-7; **26a**, 122592-23-8; **26b**, 122592-24-9; **27** isomer 1, 122622-18-8; **27** isomer 2, 122672-67-7; **28**, 122622-19-9; **29**, 122672-68-8; **30a**, 122622-20-2; **30b**, 122622-21-3; **31**, 122592-25-0; **32** isomer 1, 122622-22-4; **32** isomer 2, 122672-69-9; **33b** isomer 1, 122622-23-5; **33b** isomer 2, 122672-70-2; **33c**, 122622-24-6; **34**, 122592-27-2; **35**, 122622-25-7; **36**, 122672-71-3; **37**, 122622-26-8; **38a**, 122672-72-4; **38b**, 122622-27-9; **38c**, 122622-28-0; **38d**, 122622-29-1; **39**, 122592-28-3; $(EtO)_2POCH_2CO_2Et$, 867-88-9; $TMSCH_2CO_2Et$, 4071-88-9; $(EtO)_2POCH(CH_3)CO_2Et$, 3699-66-9; $CH_3C(OMe)_2NMe_2$, 18871-66-4; $(EtO)_2POCH_2COH_3$, 1067-71-6; propargyl bromide, 106-96-7; triethyl orthoacetate, 78-39-7; triethyl orthopropionate, 115-80-0.

Spiro-Fused 2,5-Cyclohexadienones from the Thermal 1,3-Alkyl Migrations of Quinol Vinyl Ethers. A Strategy for Conversion of a Carbonyl Carbon to a Quaternary Carbon

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Reaction of *p*-benzoquinone monoketals with 2-lithio derivatives of acetophenone and propiophenone dimethyl ketals results in organolithium addition to the carbonyl group of the quinone monoketal to afford the ketals of 4-aryl-4-hydroxy-2,5-cyclohexadienones. Reaction of these products with aqueous acid results in hydrolysis of the 2,5-cyclohexadienone ketal and intramolecular mixed ketal formation between the 4-hydroxyl group and the 2-substituted acetyl or propionyl side chain of the aromatic ring. Conversion of this cyclic ketal to the vinyl ether by loss of methanol affords the quinol ether derivatives for thermolysis. Variants of this chemistry were used to prepare a number of spiro-fused vinyl ethers of the *p*-quinols. At 130-170 °C these molecules undergo high-yield conversion of the vinyl ether moiety to a ketone, affording spiro-fused 4,4-disubstituted 2,5-cyclohexadienones. Rates have been measured for several of these formal [1,3]-shifts, and a ρ value of -0.87 was calculated for rearrangement of compounds having aryl substituents on the vinyl ether double bond. This chemistry establishes a high-yield strategy for conversion of *p*-benzoquinone monoketals, 4,4-dialkoxy-2,5-cyclohexadienones, to spiro-fused 2,5-cyclohexadienones.

Introduction

Thermally induced alkyl shifts from carbon to oxygen as represented by the Claisen rearrangement have been widely studied from both the mechanistic and synthetic viewpoints.[1] The importance of this reaction in synthesis is undoubtedly associated with the stereochemical control of, and moderate temperatures required for, this symmetry-allowed [3,3]-sigmatropic shift. Claisen[2,3] in 1896 also reported that the thermal rearrangement of 1-alkoxy-

(1) For reviews, see: (a) Tarbell, D. S. *Chem. Rev.* **1940**, *27*, 495. (b) Tarbell, D. S. *Org. React.* **1944**, *2*, 1. (c) Jefferson, A.; Scheinman, F. *Q. Rev. Chem. Soc.* **1968**, 22, 391. (d) Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1. (e) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227.

(2) (a) Claisen, L. *Chem. Ber.* **1896**, *29*, 2931. (b) Claisen, L.; Hasse, E. *Ibid.* **1900**, *33*, 3778. (c) Claisen, L. *Ibid.* **1912**, *45*, 3157.

(3) For related reaction in the older literature, see: (a) Wislecenus, W.; Schrotter, R. *Ann. Chem.* **1921**, *424*, 215. (b) Staudinger, H.; Rudzicka *Helv. Chim. Acta* **1924**, *7*, 386.

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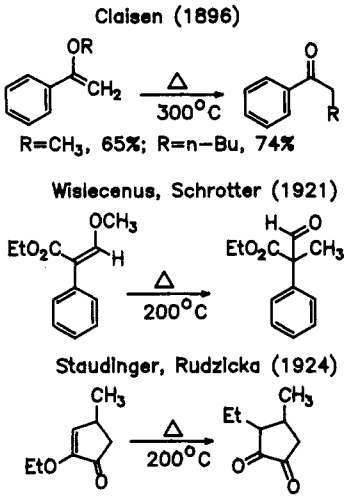
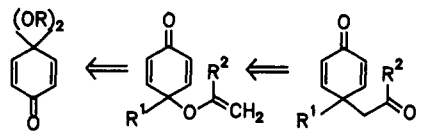
Scheme I. Selected Vinyl Ether–Ketone Conversions



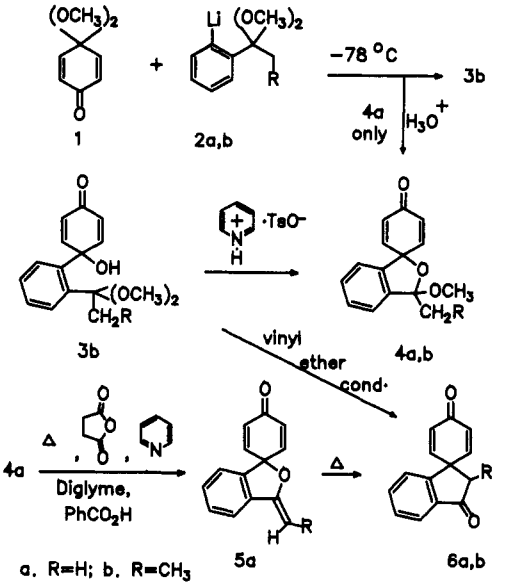
Scheme II. General Route for Conversion of Quinone Monoketals to 2,5-Cyclohexadienones



styrene derivatives in the temperature range 200–300 °C afforded the substituted acetophenones with the ease of rearrangement qualitatively following the order *n*-propyl > ethyl > methyl (Scheme I). Cross-over experiments,[4] the effect of free-radical initiators on the reaction,[5] and the loss of chirality associated with the rearrangement of a chiral substrate[5] supported a free-radical chain mechanism for the reaction. However, different mechanisms for the reaction may operate, depending on the compound and reaction conditions. Although representing a novel method for the formation of carbon–carbon bonds, this uncatalyzed thermal [1,3]-alkyl shift has invoked little synthetic interest through the years.[6,7] Certainly, the high temperatures required for reaction, the formation of side products arising from free-radical intermediates, and the reluctance of some vinyl ethers to undergo the reaction[8] have contributed to this disinterest.

Quinone monoketals are readily available intermediates[9] which can be transformed into quinol derivatives by reaction with an organolithium compound followed by ketal hydrolysis.[9] If the C-4 carbon–oxygen bond of a quinol derivative could be converted to a carbon–carbon bond in high yield under mild conditions, a versatile synthesis of the 2,5-cyclohexadienone derivative would result. One method envisioned for the process would be a formal [1,3]-shift of vinyl ether derivatives as depicted in Scheme II.[10] It was hoped that the highly stabilized intermediates (for example, phenoxy type radicals) which would be involved in a stepwise oxygen-to-carbon migration would lower the temperature (200–300 °C) of the rearrangement typically required in earlier studies.

Scheme III. Preparation and Thermal Rearrangement of Spiro Vinyl Ethers



Synthetic and Thermal Chemistry Studies

Vinyl ethers of the general structure shown in Scheme II could react via both a [3,3]-sigmatropic shift mechanism (the Claisen rearrangement) to produce α-alkylated phenols and the [1,3]-shift process (Scheme II). To minimize this problem in these exploratory studies, vinyl ether **5a**, which is incapable of a facile [3,3]-sigmatropic shift, was chosen for study. In addition, the [1,3]-shift in this system would be intramolecular. The key step in the preparation of **5a** was reaction of **1** with the lithio derivative of the dimethyl ketal of *o*-bromoacetophenone, **2a** (Scheme III). Mild acid hydrolysis of the crude product gave **4a** (78% overall). Reaction of **4a** with a mixture of succinic anhydride, pyridine, and benzoic acid in diglyme at 110 °C for 2 h gave the vinyl ether **5a** (50%).[11]

When a degassed solution of **5a** was heated to 170 °C for 18 h, a quantitive yield of **6a** resulted. Subsequent kinetic studies indicated that the preparative rearrangement of **5a** could have been done at ≃ 150 °C with about the same reaction time. The structure of **6a** was supported by the AB quartet centered at δ 6.6 ($\Delta\nu$ = 34 Hz, J_{AB} = 10 Hz) in the ^{1}H NMR spectrum, typical of the 2,5-cyclohexadienone vinyl hydrogens, and signals in the ^{13}C NMR spectrum at δ 201.9 and 185 ppm, indicative of indanone and dienone carbonyl groups.

(4) (a) Lauer, W. M.; Spielman, M. A. *J. Am. Chem. Soc.* **1933**, *55*, 4923. (b) Mortenson, C. W.; Spielman, M. A. *J. Am. Chem. Soc.* **1940**, *62*, 1609.

(5) (a) Wiberg, K. B.; Rowland, B. I. *J. Am. Chem. Soc.* **1955**, *77*, 1159. (b) Wiberg, K. B.; Shryne, T. M.; Kinter, R. R. *Ibid.* **1957**, *79*, 3160. (c) Wiberg, K. B.; Kinter, R. R.; Motell, E. L. *J. Am. Chem. Soc.* **1963**, *85*, 450.

(6) For related reactions in aromatic and heterocyclic chemistry, see: (a) Elkobaisi, F. M.; Hickinbottom, W. J. *J. Chem. Soc.* **1959**, 1873. (b) Hart, H.; Eleuterio, H. S. *J. Am. Chem. Soc.* **1954**, *76*, 519 and references cited therein. (b) Stirling, C. J. M. *J. Chem. Soc.* **1960**, 255. (c) For a short review of thermal [1,3]-alkyl shifts, see: Dalrymple, D. L.; Kruger, T. L.; White, W. N. *Chemistry of the Ether Linkage*; Patai, S., Ed.; John Wiley: New York, 1967; Chapter 14, pp 660–663. Landis, P. S. *Mechanism of Molecular Migrations*; Thyagarajan, B. S., Ed.; John Wiley: New York, 1968; pp 43–63.

(7) Palladium-catalyzed [1,3]-shifts of enol ethers of β-dicarbonyl systems are formally related to these reaction but proceed via different mechanistic pathways: Trost, B. M.; Runge, T. A.; Jungheim, L. N. *J. Am. Chem. Soc.* **1980**, *102*, 2840. Trost, B. M.; Runge, T. A. *J. Am. Chem. Soc.* **1981**, *103*, 7550; **1981**, *103*, 7559.

(8) (a) Wislecenus, W. *Chem. Ber.* **1900**, *33*, 1469. (b) Pauley, H.; Lieck, H. *Ibid.* **1900**, *33*, 3157. (c) Powell, S. G.; Adams, R. *J. Am. Chem. Soc.* **1920**, *42*, 646. (d) Lauer, W. M.; Spielman, M. A. *Ibid.* **1933**, *55*, 1572.

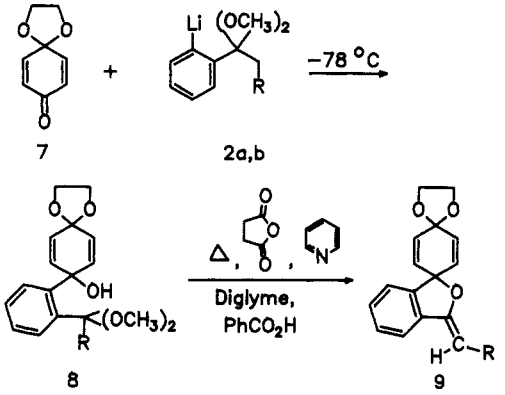
(9) For reviews and leading references, see: (a) Swenton, J. S. *Acc. Chem. Res.* **1983**, *16*, 74. (b) Swenton, J. S. *The Chemistry of Quinonoid Compounds*; Rappoport, Z., Patai, S., Eds.; John Wiley: New York, 1988; Part 2, p 899.

(10) Some of this work has been presented at the *Third Chemical Congress of North America*, Toronto, Canada, June 5–10, 1988, paper no. 352 and a preliminary report has appeared: Morrow, G. W.; Wang, S.; Swenton, J. S. *Tetrahedron Lett.* **1988**, *29*, 3441.

(11) These were essentially the conditions of Newman, M. S.; Zwander Zwan, M. C. *J. Org. Chem.* **1973**, *38*, 2910.

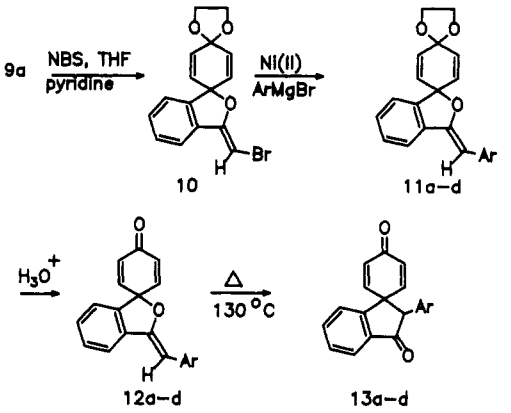
The chemistry proceeded similarly for the propiophenone derivative except that **4b** was not formed directly from the reaction of **1** and **2b**. First, the product from the reaction of **2b** with **1** was hydrolyzed to the quinol **3b** followed by intramolecular ketal formation in a second step to give **4b**. It was difficult to effect a clean conversion of **4b** to **5b** since under the conditions for the **4b** → **5b** transformation, the vinyl ether **5b** underwent partial rearrangement to the diketone **6b**. For preparative purposes, heating **3b** with a mixture of succinic anhydride, pyridine, and benzoic acid gave **6b** (52%) in one step. This method should serve as a general route to spiro dienones having alkyl substituents on the five-membered ring. To obtain pure **5b** required for kinetic studies to be presented later, the diketone derived from acid hydrolysis of the quinol **3b** was converted to **5b** (see the Experimental Section).

Since the vinyl ether-to-ketone conversion efficiently forms a spiro-fused ring system from readily available materials, a more general method for preparation of vinyl ethers for rearrangement was briefly investigated. The acid sensitivity of the dimethyl ketal used in this initial work mitigated against the use of one of the intermediates in Scheme III in a more general approach to the spiro vinyl ether moiety for thermal rearrangement. Thus, a similar synthetic route to the ethylene ketal derivatives **9a,b** was developed using the ethylene monoketal **7**.



Compound **9a** contains chemically differentiated dienone and vinyl ether units and could serve as the intermediate in a convergent route to spirodienone vinyl ethers. Bromination of **9a** afforded the bromide **10** in 70% yield. In principle, the bromo substituent could be replaced with a number of alkyl/aryl groups by the use of appropriate organometallic reagents. Only the coupling of **10** with aryl Grignard reagents was studied since this produced the required systems for a substituent-effect study to be described later. The dichloro[1,3-bis(diphenylphosphino)-propane]nickel(II)-catalyzed coupling[12] of **10** with phenyl-, (*p*-methoxyphenyl)-, (*p*-methylphenyl)-, and (*p*-(trifluoromethyl)phenyl)magnesium bromide gave the respective vinyl ethers **11a–d**. Since a major side reaction in this process is coupling of the Grignard reagent to give the corresponding biphenyl, 2–3 equiv of Grignard reagents were employed to obtain 50–60% yields of **11a–d**.

The questionable step in the synthesis was the selective deblocking of the ethylene ketal in the presence of the vinyl ether moiety. Since these two functionalities are hydrolyzed by different acid-catalyzed mechanisms,[13] it was



a. Ar=C_6H_5; b. Ar=p-$CH_3OC_6H_4$; c. Ar=p-$CH_3C_6H_4$; d. Ar=p-$CF_3C_6H_4$

hoped that selectivity could be achieved in this step. Stirring compounds **11a–d** in dilute hydrochloric acid/tetrahydrofuran did give the required dienone vinyl ethers **12a–d** in >90% yields. Heating these vinyl ethers in degassed solvents at 110–130 °C afforded the corresponding [1,3]-shift products **13a–d** in good yield.

Mechanistic Studies

A number of mechanisms—free-radical chain reactions, biomolecular alkyl transfers, and concerted rearrangements—have been proposed for thermal [1,3]-shifts recorded in the older literature. A bimolecular mechanism and a free-radical chain process are unlikely for the reactions reported herein. Although this rearrangement was originally envisioned as occurring via a stepwise biradical process, a concerted reaction cannot be rigorously excluded. However, the effect of solvent and structural modification of the vinyl ether on the rate of the reaction would furnish some quantitative information on the mechanism of the [1,3]-shift.

The kinetics for rearrangement of the vinyl ethers **5a,b** were measured by conducting the reactions in degassed sealed tubes in benzene solvent and monitoring the formation of product by ^1H NMR spectroscopy (see the Experimental Section for details). For the phenyl-substituted systems **12a–d**, the progress of the sealed-tube reactions was followed by monitoring the disappearance of the starting material by UV spectroscopy. The results of these determinations are given in Table I.

An initial point for discussion is the degree of charge separation associated with the vinyl ether-to-ketone rearrangements. One method for assessing charge separation in the transition state of the rearrangement would be the effect of solvent on the rate of the **5a** → **6a** rearrangement. The **5a** → **6a** reaction occurs in nearly quantitative yield in benzene. However, in polar solvents such as acetonitrile, methanol, ethanol, and nitromethane, a dark purple mixture results. Although **6a** was formed in the reaction as shown by ^1H NMR analysis of the crude product, other unidentified products were present, and measurements of the rate constants in these solvents were deemed to be unreliable. A control experiment showed that when **6a** was heated in methanol at 153 °C, a dark purple color developed, suggesting that product instability under the reaction conditions rather than a solvent effect on the **5a** → **6a** reaction was responsible for the above result.[15] However, rates determined in *tert*-butyl alcohol (E_T = 43.9)[16] were

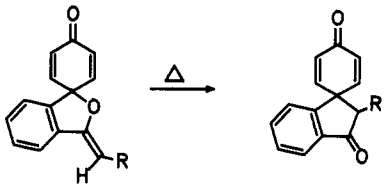
(12) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374. Kumada, N. *Pure Appl. Chem.* **1980**, *52*, 669. Kumada, M.; Tamao, K. *Org. Synth.* **1978**, *58*, 127.

(13) Alder, R. W.; Baker, R.; Brown, J. M. *Mechanism in Organic Chemistry*; Wiley Interscience: New York, 1975; pp 64–67.

(14) These numbers differ by a factor of 2.3 from those previously reported due to a mathematical error in the earlier calculations.

(15) Although this reaction has not been investigated, the chemistry is probably initiated by intramolecular addition of the enol form of the ketone to the dienone unit.

Table I. Rate Constants[a] ($\times 10^5$ s^{-1}) for Thermal Rearrangements of Spiro Vinyl Ethers[14]



	R					
T, °C	H[b]	CH_3	p-$OCH_3C_6H_4$	p-$CH_3C_6H_4$[c]	C_6H_5	p-$CF_3C_6H_4$
99	-	-	13.9	4.87	2.63	0.87
113	-	-	-	-	12.3	-
128	-	-	-	-	51.8	-
153	2.60	37.9	-	-	494[d]	-
169	10.6	-	-	-	-	-
182	32.4	-	-	-	-	-

[a] Averages of two determinations with an estimated accuracy of ±5%. [b] For R = H; $k = kT/he^{-31800/RT}e^{-5.5/R}$. [c] For R = Ph; $k = kT/he^{-29700/RT}e^{-0.1/R}$. [d] Calculated from temperature dependence of the rate.

nearly identical with the rates measured in benzene (E_T = 34.5),[16] suggesting that there is no pronounced charge separation subject to solvation. *These studies did establish that the choice of solvent is important in obtaining a clean, high-yield rearrangement reaction in these systems.*

The ρ value would be another criterion for assessing charge separation in these [1,3]-shift reactions. The kinetic data (Table I) show that replacement of a hydrogen on the vinylic carbon with a phenyl group increases the rate constant at 153 °C by about 200. Thus, the rate constants for a series of para-substituted phenyl systems (Table I) were measured and correlated with both σ and σ^+ parameters. The correlation with σ^+ was excellent (ρ = −0.87, correlation coefficient = 0.998) while the correlation with σ was much poorer (ρ = −1.13, correlation coefficient = 0.94). *The modest magnitude of the ρ value argues against a mechanism involving charged intermediates.* However, it does not distinguish between a stepwise and a concerted process, both of which give ρ values in this range when correlated with σ^+.[17]

The difficult question of whether the reaction proceeds in a stepwise manner involving biradical intermediates or via a concerted reaction with inversion of configuration at a reacting center cannot be answered here. Crude calculations place the energy required for homolytic cleavage of the carbon–oxygen bond of **5a** at ≃35.4 kcal/mol.[18] Since the activation energy for the thermolysis of **5a** is ≃32 kcal/mol, it is possible that the reaction does possess some concerted character. Furthermore, replacement of a hydrogen on the vinyl carbon by a phenyl group leads to ≃2 kcal/mol reduction in the activation energy, whereas benzylic radical stabilization is usually on the order of 12–15 kcal/mol.[21] Unfortunately, we are unaware of the magnitude of phenyl stabilization on an acetonyl radical. In addition, the C–O bond being broken in the reaction is orthogonal to the π-orbitals of both the fused aromatic ring and the vinyl ether double bond. However, substitution on the vinyl carbon does affect the rate constant for the reaction. This could result from interaction of the nonbonding oxygen electrons with the olefinic system or some twisting in the transition state for rearrangement. The effect of the fused aromatic ring on the chemistry could be different since not only are the p orbitals of the ring orthogonal to the C–O bond, but also the ring is at the nodal carbon of the acetonyl species being generated. *This latter consideration suggests that compounds lacking the fused aromatic ring should undergo the [1,3]-shift reaction with equal facility to those reported herein.*

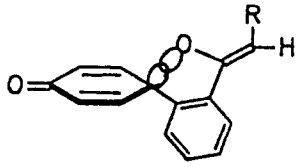


Figure 1. Orthogonality of the aromatic and olefinic groups vs the C-4 carbon–oxygen bond.

The spirodienones formed in these thermal reactions have both dienone and indanone linkages which could be transformed to other functional groups. The success of this conversion would depend on selective chemical reactivity of one of the carbonyl groups. Another approach to selective conversion of the carbonyl groups in these products would be to prepare the spirodienones with the two carbonyl groups differentiated chemically. In fact, **9b** could be arranged to **14** (49% yield) in *o*-dichlorobenzene heated to reflux. However, attempts to rearrange analogous vinyl ethers **9a** or **11a** under similar reaction conditions led either to no reaction or to complex reaction mixtures. Other methods are being explored for effecting the vinyl ether-to-ketone conversion in componds wherein the two carbonyl groups would be differentiated.

Although major mechanistic questions remain unanswered, this work has demonstrated the viability of converting quinone monoketals to 4,4-substituted 2,5-cyclohexadienones. *The rates of the rearrangement of **5** and*

(16) (a) Reichardt, C. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 29. (b) Reichardt, C. *Justus Liebigs Ann. Chem.* **1971**, *64*, 752.

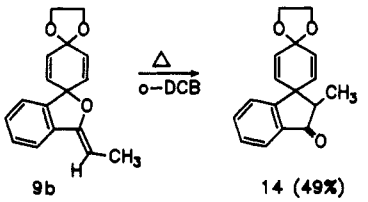
(17) (a) Alfassi, Z. B. *Chemical Kinetics of Small Organic Radicals*; CRC Press; Boca Raton, FL, 1988; Vol. 2, p 64. (b) DeWitt, E. J.; Lester, C. T.; Ropp, G. A. *J. Am. Chem. Soc.* **1956**, *78*, 2101.

(18) This value was determined by subtracting: the resonance energy of the phenoxy radical (O-H bond energy of water–phenol = 34 kcal/mol), the resonance energy of the acetonyl radical[19] (≃8.6 kcal/mol), and the strain energy of cyclopentene[20] (≃6 kcal/mol) from the energy of a carbon–oxygen single bond (84 kcal/mol). A reviewer has noted that the use of the O-H bond energies and resonance effects neglects polar effects that need not be present when hydrogen is replaced by carbon. Furthermore using the resonance energy of the acetonyl radical in the calculation is an approximation. We agree with those comments and as indicated in the text present these values as only crude approximations since, to our knowledge, bond energy of similar linkages have not been measured.

(19) For leading references, see: Camaioni, D. M.; Walter, H. F.; Jordan, J. E.; Pratt, D. W. *J. Am. Chem. Soc.* **1973**, *95*, 7978. Huyser, E. S.; Feller, D.; Borden, W. T.; Davidson, E. R. *J. Am. Chem. Soc.* **1982**, *104*, 2956.

(20) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper and Row: New York, 1981; p 150.

(21) Calculated by subtracting the C–H bond energy of ethane from the benzylic C–H bond energy of toluene.



12 together with stereoelectronic considerations suggest that compounds lacking the aryl group at C-4 of the quinol ether will undergo rearrangement at moderate temperature. Perhaps this formal [1,3]-shift can even compete with the well-known [3,3]-sigmatropic shift in unconstrained systems. *This general strategy for converting a carbonyl carbon to a quaternary carbon via organolithium addition followed by vinyl ether rearrangement could have utility in other systems.* Additional studies are in progress and will be reported at a later date.

Experimental Section[22]

***o*-Bromoacetophenone Dimethyl Ketal.** To a solution of *o*-bromoacetophenone (5.0 g, 25.1 mmol) in CH_3OH (25 mL) were added trimethyl orthoformate (5 mL) and *p*-TsOH (50 mg), and the resulting solution was stirred for 6 h. After being neutralized with 1% KOH/CH_3OH (10 mL), the solvent was removed in vacuo, and the product was dissolved in $CHCl_3$ (100 mL). Workup and distillation of the residue afforded the ketal (6.0 g, 97%) as a water white oil: bp 93–95 °C (0.4 mm); IR (NaCl) 2990 (m), 2940 (br, m), 2830 (m), 1460 (m), 1428 (m), 1371 (m), 1280 (m), 1245 (m), 1189 (m), 1140 (m), 1095 (m), 1050 (m), 1035 (m), 1020 (m), 875 (m), 755 (m); ^1H NMR δ 7.9–7.0 (m, 4 H), 3.2 (s, 6 H), 1.6 (s, 3 H); mass spectrum, exact mass calcd for $C_{10}H_{13}O_2Br$ m/e 246.0078, obsd 246.0080.

Preparation of 4a. To a solution of the above dimethyl ketal (2.5 g, 10.2 mmol) in THF (25 mL) at −78 °C was added dropwise *n*-BuLi (7.0 mL of a 1.6 M solution, 11.2 mmol) over 10 min, and the solution was stirred for 2 h at this temperature. To the resulting milky suspension was added dropwise 4,4-dimethoxy-2,5-cyclohexadienone (1)[23] (1.6 g, 10.4 mmol) in THF (5.0 mL) over 10 min, and the solution was stirred at −78 °C for 1 h and allowed to warm to room temperature. After the reaction was quenched with saturated aqueous NH_4Cl (5.0 mL), extractive workup using Et_2O (100 mL) gave the crude quinol ketal. This material was dissolved in $(CH_3)_2CO$ (75 mL), 8% aqueous HOAc (15 mL) was added, and the solution was stored at 0 °C for 16 h. After concentration in vacuo, extractive workup using CH_2Cl_2 (2 × 75 mL) gave **4a** (1.9 g, 78%) as a white solid, mp 145–151 °C, which was deemed suitable for use in the next step without further purification. Recrystallization of a portion from Et_2O gave the analytically pure material: mp 161–162 °C; IR (KBr) 1672 (vs), 1630 (m), 1170 (m), 1065 (m), 1025 (m), 870 (m), 841 (m), 770 cm^{-1} (m); ^1H NMR δ 7.6–7.2 (m, 3 H), 7.2–6.5 (highly str m, 3 H), 6.24 (d, J = 9 Hz, 2 H), 3.25 (s, 3 H), 1.83 (s, 3 H); mass spectrum, exact mass calcd for $C_{15}H_{14}O_3$ m/e 242.0943, obsd m/e 242.0942.

Preparation of 5a. A solution of succinic anhydride (715 mg) and benzoic acid (13 mg) in a mixture of pyridine (2.0 mL) and diglyme (2.0 mL) was stirred and heated at 110 °C for 15 min, after which time **4a** (1.0 g, 4.1 mmol) was added all at once. The resulting clear solution was heated and stirred for 2 h, but TLC analysis (2:1 PE/Et_2O) indicated remaining **4a**. Additional succinic anhydride (50 mg) was added, and the mixture was heated and stirred for an additional 30 min and then allowed to cool to room temperature. The crude reaction mixture was then poured into saturated aqueous $NaHCO_3$ (50 mL). Extractive workup using Et_2O (75 mL) gave a brown oil, which was chromatographed on silica gel (6 in. × 1 in. column, 10% Et_2O/PE as eluant) to afford the vinyl ether **5a** (0.431 g, 50%) as a fluffy white solid: mp 89–91 °C; IR (KBr) 1671 (vs), 1630 (s), 1466 (m), 962 (m), 761 cm^{-1} (m); ^1H NMR δ 7.6–7.0 (str m, 4 H), 6.5 (AB q, $\Delta\nu$ = 40 Hz, J_{AB} = 10 Hz, 4 H), 4.65 (q, J = 3 Hz, 2 H); mass spectrum, exact mass calcd for $C_{14}H_{10}O_2$ m/e 210.0681, obsd m/e 210.0693.

Thermal Rearrangement of 5a and Preparation of 6a. A solution of **5a** (250 mg, 1.0 mmol) in freshly distilled benzene (25 mL) was placed in a heavy-walled Pyrex tube and degassed by three freeze–thaw cycles. After being sealed under N_2, the tube was heated at 170 °C for 18 h. Concentration of the solution gave a light tan solid **6a** (250 mg, 99%), which had mp 184–188 °C (dec) and spectroscopic properties identical with purified material. Attempts to purify this material by chromatography on silica gel or neutral alumina resulted in rapid decomposition to a blue oil of unknown composition. Recrystallization from Et_2O gave a white solid, which darkened at 187 °C and melted at 188–190 °C (dec), leaving a dark purple liquid: IR (KBr) 1710 (vs), 1667 (vs), 1628 (m), 1598 (m), 1405 (m), 1232 (m), 858 (m), 765 cm^{-1} (m); ^1H NMR δ 8.0–7.2 (highly str m, 4 H), 6.6 (AB q, $\Delta\nu$ = 34 Hz, J_{AB} = 10 Hz, 4 H), 2.9 (s, 2 H); ^{13}C NMR δ 201.9, 185.0, 153.5, 151.0 (2 C), 135.7, 129.5, 128.4 (2 C), 127.1, 125.8, 124.8, 47.5, 46.7; mass spectrum, exact mass calcd for $C_{14}H_{10}O_2$ m/e 210.0681, obsd 210.0681.

***o*-Bromopropiophenone.** Fresh *o*-bromobenzoyl chloride was prepared in the usual fashion by treatment of *o*-bromobenzoic acid (25 g, 0.124 mol) with thionyl chloride (30 mL) and a catalytic amount of dimethylformamide (0.1 mL) at reflux for several hours. Distillation afforded the acid chloride (25.3 g, 93%) as a light yellow oil, bp 135–140 °C (20 mm) (lit.[24] bp 181–182 °C (125 mm)), which was used directly in the next step.

A solution of the above acid chloride (3.0 g, 13.7 mmol) in THF (30 mL) was cooled to −78 °C, and an ethereal solution of ethylmagnesium bromide (7.34 mL, 14.7 mmol) was added over 0.5 h. The reaction mixture was allowed to warm to room temperature and was stirred for an additional 4 h. Addition of saturated aqueous NH_4Cl (20 mL) gave two layers, the organic layer was separated and concentrated, and the residue was partitioned between Et_2O and water. Workup and drying (Na_2SO_4) gave a light yellow oil, which was distilled to afford the colorless ketone (2.6 g, 89%), bp 85–89 °C (1 mm), no lit.[25] boiling point given.

***o*-Bromopropiophenone Dimethyl Ketal.** To a solution of *o*-bromopropiophenone (6.5 g, 30.5 mmol) in CH_3OH (35 mL) were added trimethyl orthoformate (7 mL) and *p*-TsOH (15 mg), and the resulting mixture was stirred at room temperature for 12 h. Solid KOH (0.1 g) was added and allowed to dissolve, the mixture was concentrated in vacuo, and the product was extracted into Et_2O (2 × 50 mL). Standard workup gave a light yellow oil, which was distilled at reduced pressure to afford the title compound (7.2 g, 91%) as a water-white oil: bp 115–118 °C (0.4 mm); IR (NaCl) 2985 (m), 2940 (m), 2825 (m), 1468 (m), 1430 (m), 1298

(22) Melting points were determined in capillaries in a Thomas-Hoover "Unimelt" apparatus and are uncorrected. IR spectra were determined on a Perkin-Elmer Model 283B spectrometer in KBr pellets or neat using NaCl plates with only strong (s) and medium (m) intensity bands reported. Routine ^1H NMR spectra (ppm) were determined at 80 MHz on an IBM NR 80 spectrometer using deuteriochloroform as solvent and residual chloroform as standard. Signals having sharply defined lines for which analysis of the coupling constants were not extracted are characterized as str. All ^{13}C NMR spectra were determined at 20 MHz on the above instrument. Mass spectral and exact mass measurements were obtained by Richard Weisenberger on a Kratos MS-30 spectrometer connected to a DS-55 data system. Combustion analyses were performed by Scandinavian Microanalytical Laboratory, Herlev, Denmark. All reagents or compounds not explicitly referenced were obtained from the Aldrich Chemical Co. Alumina and silica gel (Kieselgel 60 230–400 mesh) were obtained from E. Merck Co. Thin-layer chromatography (TLC) was done using Merck silica gel 60 F_{254} precoated aluminum backed plates, 0.2-mm thickness. Visualization was by UV or by spraying with 5% ethanolic phosphomolybdic acid and then heating. Tetrahydrofuran was purified by distillation from benzophenone ketyl. All organometallic reactions were done under nitrogen or argon. Throughout the Experimental Section the following abbreviations are used: petroleum ether, bp 35–60 °C (PE), tetrahydrofuran (THF), *p*-toluenesulfonic acid (*p*-TsOH), and thin-layer chromatography (TLC). 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).

(23) This compound is commercially available, but expensive; it can be easily prepared on a 50-g scale via the chemistry described in: Henton, D. R.; Anderson, K.; Manning, M. J.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 3422. Henton, D. R.; McCreery, R. L.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 369.

(24) Adams, R.; Ulich, L. H. *J. Am. Chem. Soc.* **1920**, *42*, 599.

(25) Boger, D. L.; Duff, S. R.; Panek, J. S.; Yasuda, M. *J. Org. Chem.* **1985**, *50*, 5782.

(26) Dolson, M. G.; Swenton, J. S. *J. Org. Chem.* **1981**, *46*, 177.

(m), 1185 (m), 1150 (m), 1130 (m), 1110 (m), 1090 (m), 1060 (m), 1025 (m), 950 (m), 759 cm^{-1} (m); ^1H NMR δ 7.9–7.5 (str m, 2 H), 7.5–7.1 (str m, 2 H), 3.23 (s, 6 H), 2.24 (q, J = 7 Hz, 2 H), 0.6 (t, J = 7 Hz, 3 H). Anal. Calcd for $C_{11}H_{15}O_2Br$: C, 50.98; H, 5.79. Obsd: C, 51.56; H, 5.76.

Preparation of 3b. To a solution of the above ketal (4.0 g, 15.4 mmol) in THF (50 mL) at −78 °C was added dropwise *n*-BuLi (11.2 mL of a 1.45 M solution, 16.4 mmol). After being stirred at this temperature for 2 h, a solution of 4,4-dimethoxy-2,5-cyclohexadienone (1)[23] (2.37 g) in THF (10 mL) was added dropwise. The resulting mixture was stirred for 1 h and allowed to warm to room temperature over 12 h, and the reaction was then quenched with a saturated aqueous NH_4Cl solution (15 mL). Extractive workup using Et_2O (100 mL) gave a crude product, which was dissolved in $(CH_3)_2CO$ (150 mL) and cooled to −12 °C. Cold 5% aqueous HOAc (50 mL) was added, and the homogeneous mixture was stored in a freezer at −12 °C for 24 h. Addition of a saturated aqueous $NaHCO_3$ solution (50 mL) followed by concentration in vacuo afforded a dark oil, which slowly solidified upon standing. Crystallization from Et_2O/PE gave in two crops **3b** (1.85 g, 43%) as white crystals: mp 99–101 °C; IR (KBr) 3362 (m), 1670 (s), 1090 (m), 1058 (m), 1030 (s), 955 (m), 859 (m), 751 cm^{-1} (m); ^1H NMR δ 7.7–7.3 (str m, 4 H), 6.4 (AB q, $\Delta\nu$ = 65 Hz, J_{AB} = 10 Hz, 4 H), 3.29 (s, 6 H), 2.2 (q, J = 8 Hz, 2 H), 0.75 (t, J = 8 Hz, 3 H); mass spectrum, exact mass calcd for $C_{17}H_{20}O_4$ m/e 288.1362, obsd m/e 288.1324.

Preparation of 4b. To a solution of **3b** (0.5 g, 1.7 mmol) in CH_2Cl_2 (200 mL) was added pyridinium *p*-toluenesulfonate[27] (10 mg), and the resulting mixture was stirred for 10 min and then poured into saturated $NaHCO_3$ (100 mL). Workup gave a residue, which was dissolved in a minimum of Et_2O/PE and allowed to crystallize. The cyclic ketal **4b** (0.2 g, 45%) was obtained as a white solid, mp 108–111 °C. Repeated crystallization from Et_2O/PE gave the analytically pure material: mp 112–114 °C; IR (KBr) 1662 (s), 1632 (m), 1068 (m), 1030 (m), 910 cm^{-1} (m); ^1H NMR δ 7.5–7.3 (m, 3 H), 7.2–6.7 (m, 3 H), 6.3 (d, J = 10 Hz, 2 H), 3.24 (s, 3 H), 2.1 (pseudooctet, J = 7 Hz, 2 H), 1.0 (t, J = 7 Hz, 3 H). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Obsd: C, 74.84; H, 6.37.

In Situ Generation and Thermal Rearrangement of 5b, Preparation of 6b. To a solution of **3b** (0.25 g, 0.87 mmol) in a mixture of pyridine (2.5 mL) and diglyme (2.5 mL) were added succinic anhydride (0.5 g) and benzoic acid (5 mg), and the resulting mixture was heated at 160 °C for 8.5 h. After being cooled, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (25 mL). Extractive workup using Et_2O (3 × 25 mL) was followed by removal of the residual pyridine and diglyme in vacuo (0.2 mm Hg) over 12 h. This residue was dissolved in a minimum of CH_3OH and allowed to slowly crystallize at 0 °C. Filtration and drying in vacuo afforded spirodienone **6b** (0.075 g) as a light yellow solid, mp 143–145 °C. The mother liquors from the above crystallization were chromatographed on silica gel (6 in. × $^1/_4$ in. column, 10% EtOAc/PE as eluant) to afford additional **6b** (0.025 g), mp 143–145 °C (0.100 g total, 52%). Repeated crystallization of a portion from Et_2O/PE gave the analytically pure material as white crystals: mp 149–150 °C; IR (KBr) 1721 (s), 1662 (s), 1621 (m), 1598 (m), 1460 (m), 1408 (m), 1222 (m), 855 cm^{-1} (m); ^1H NMR δ 7.7–7.1 (highly str m, 4 H), 7.0–6.2 (highly str m, 4 H), 2.95 (q, J = 7 Hz, 1 H), 1.14 (d, J = 7 Hz, 3 H); ^{13}C NMR (20 MHz) δ 204, 185.4, 152, 150.5, 150.2, 135.4, 130.2, 129.4, 128.8, 125.4, 124.9, 53.0, 52.2, 10.0 (one C missing). Anal. Calcd for $C_{15}H_{12}O_2$: C, 80.34; H, 5.35. Found: C, 80.09; H, 5.47.

Preparation of 8a. To a solution of *o*-bromoacetophenone dimethyl ketal (15.0 g, 61.2 mmol) in THF (150 mL) at −78 °C was added *n*-BuLi (43 mL of 1.45 M solution, 63.2 mmol) dropwise over 15 min, and the resulting mixture was stirred for 2 h. A solution of *p*-benzoquinone monoethylene ketal (7)[26] (9.3 g, 61.8 mmol) in THF (30 mL) was added dropwise, stirring was continued at −78 °C for 1 h, and the solution was then allowed to warm to room temperature over 2 h. The reaction was quenched with water (125 mL), and extractive workup using Et_2O (300 mL) gave an oily solid, which was triturated with Et_2O/PE and filtered to afford **8a** (15.2 g, 79%) as a white solid, mp 95–98 °C. This material was suitable for use in the next step. Recrystallization of a portion from Et_2O/PE gave the analytical sample: mp 103–106 °C; IR (KBr) 3370 (m), 1450 (m), 1380 (m), 1190 (m), 1150 (m), 1112 (s), 1040 (s), 1010 (s), 968 (s), 942 (m), 875 (m), 762 cm^{-1} (m); ^1H NMR δ 7.5–7.1 (str m, 4 H), 6.7 (s, 1 H), 6.10 (AB q, $\Delta\nu$ = 49 Hz, J_{AB} = 10 Hz, 4 H), 4.08 (s, 4 H), 3.28 (s, 6 H), 1.78 (s, 3 H). Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.91. Obsd: C, 67.94; H, 7.03%.

Preparation of 8b. To a solution of *o*-bromopropiophenone dimethyl ketal (18.2 g, 70.3 mmol) in THF (250 mL) at −78 °C was added *n*-BuLi (49.2 mL of a 1.5 M solution, 73.8 mmol) dropwise, and the resulting mixture was stirred for 2 h. A solution of *p*-benzoquinone monoethylene ketal (7)[26] (10.7 g, 70.4 mmol) in THF (50 mL) was added dropwise, and the solution was stirred at −78 °C for 1 h and then at room temperature for 12 h. After quenching the reaction with water (50 mL) and extractive workup using Et_2O (200 mL), crystallization of the residue from Et_2O/PE gave **8b** (14.8 g, 63%) in three crops as a white solid, mp 102–104 °C, which was deemed suitable for use directly in the next step without further purification. Recrystallization of a portion from Et_2O/PE gave the analytical sample: mp 105–106 °C; IR (KBr) 3345 (m), 1140 (m), 1112 (s), 1098 (m), 1058 (m), 1042 (m), 1021 (m), 970 (s), 890 cm^{-1} (m); ^1H NMR δ 7.5–7.0 (str m, 4 H), 6.85 (s, 1 H), 5.9 (AB q, $\Delta\nu$ = 38 Hz, J_{AB} = 10 Hz, 4 H), 3.95 (s, 4 H), 3.13 (s, 6 H), 2.1 (q, J = 8 Hz, 2 H), 0.6 (t, J = 8 Hz, 3 H). Anal. Calcd for $C_{19}H_{24}O_5$: C, 68.66; H, 7.28. Obsd: C, 68.56; H, 7.25.

Preparation of 9a. To a solution of **8a** (6.0 g, 18.8 mmol) in a mixture of pyridine (27 mL) and diglyme (27 mL) were added succinic anhydride (6.6 g) and benzoic acid (0.07 g), and the resulting mixture was heated and stirred at 140–150 °C for 2.5 h. After being cooled, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (125 mL), and the resulting precipitate was collected by vacuum filtration and washed with water (50 mL) to remove residual pyridine and diglyme. The moist solid was dissolved in EtOAc (100 mL), and extractive workup gave **9a** (3.95 g, 83%) as a tan solid, mp 118–121 °C, which was deemed suitable for use directly in the next step. Recrystallization of a portion from Et_2O/PE gave the analytical sample as white needles: mp 123–125 °C; IR (KBr) 1662 (m), 1470 (m), 1405 (m), 1290 (m), 1250 (m), 1115 (s), 1005 (m), 975 (m), 960 (s), 940 (m), 760 cm^{-1} (m); ^1H NMR δ 7.4–7.0 (str m, 4 H), 5.87 (s, 4 H), 4.47 (m, 2 H), 4.0 (s, 4 H); mass spectrum, exact mass calcd for $C_{16}H_{14}O_3$ m/e 254.0943, obsd m/e 254.0933.

Preparation of 9b. To a solution of **8b** (6.0 g, 18 mmol) in a mixture of pyridine (26 mL) and diglyme (26 mL) were added succinic anhydride (6.2 g) and benzoic acid (65 mg), and the resulting solution was heated at 140–150 °C for 2.5 h. After being cooled to room temperature, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (125 mL), and the resulting precipitate was collected by vacuum filtration and washed with 5% aqueous $NaHCO_3$ (2 × 50 mL). The moist solid was dissolved in EtOAc (100 mL), and extractive workup gave **9b** (3.8 g, 79%) as chunky, brown crystals, mp 108–115 °C. Recrystallization of a portion from Et_2O/PE gave the analytical sample: mp 115–117 °C; IR (KBr) 1690 (m), 1461 (m), 1405 (m), 1301 (m), 1118 (s), 1091 (m), 1006 (m), 995 (m), 970 (s), 955 (m), 942 (m), 750 cm^{-1} (m); ^1H NMR δ 7.3–7.0 (str m, 4 H), 5.87 (s, 4 H), 4.9 (q, J = 7 Hz, 1 H), 4.0 (s, 4 H), 1.73 (d, J = 7 Hz, 3 H); mass spectrum, exact mass calcd for $C_{17}H_{16}O_3$ m/e 268.1100, obsd m/e 268.1111.

Preparation of 5b. Compound **8b** (1 g, 3.0 mmol) was dissolved in THF (100 mL) and cooled to 0 °C, followed by addition of 5% HCl (10 mL) to the cold solution. The resulting homogeneous solution was stored in the refrigerator for 14 h, after which time the reaction was quenched by adding saturated aqueous $NaHCO_3$ (80 mL). Extractive workup (Et_2O, 100 mL) gave a thick light yellow oil (2 g, 96%), which was combined with diglyme (9 mL), pyridine (9 mL), succinic anhydride (2.2 g), and benzoic acid (25 mg). The resulting solution was heated at 110 °C for 5.5 h and then cooled to room temperature and poured into saturated $NaHCO_3$ (150 mL). The resulting solid was vacuum filtrated, washed with H_2O (50 mL), and dried under vacuum. The resulting tan solid (1.3 g), was chromatographed on silica gel (16 × 2.5 cm column, 5% Et_2O/PE as eluant) to give **5b** as a white solid (1.1 g, 61%). A small portion was recrystallized from Et_2O and hexane to give a white solid: mp 115–116 °C; IR (KBr) 2820–3110 (m), 1690 (s), 1670 (s), 1635 (s), 1610 (m), 1600 (m), 1470 (m), 1460

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(s), 1400 (m), 1300 (m), 1250 (m), 1170 (m), 1070 (m), 1050 (s), 1020 (m), 990 (s), 955 (m), 855 (s), 770 cm^{-1} (s); ^1H NMR δ 6.8–7.5 (m, 4 H), 6.5 (AB q, $\Delta\nu$ = 40 Hz, J_{AB} = 10 Hz, 4 H), 5.1 (q, J = 7 Hz, 1 H), 1.8 (d, J = 7 Hz, 3 H); mass spectrum, exact mass calcd for $C_{15}H_{12}O_2$ m/e 224.0838, obsd m/e 224.0842.

Preparation of 10. To a solution of **9a** (2.25 g, 6.7 mmol) in THF (100 mL) at 0 °C were added pyridine (2.0 mL) and *N*-bromosuccinimide (2.4 g, 6.8 mmol) in THF (10 mL). After 10 min, no starting material remained by TLC analysis (1:1 Et_2O/PE), and the reaction mixture was then poured into saturated aqueous $NaHCO_3$ (50 mL). Extractive workup using Et_2O (3 × 60 mL) gave a gummy residue, which was recrystallized from Et_2O/PE to afford **10** (2.1 g, 71%) as off-white crystals, mp 127–129 °C. The material can also be purified by chromatography on silica gel (20% Et_2O/PE as eluant). Recrystallization of a portion from Et_2O/PE gave the analytically pure material: mp 128–129.5 °C; IR (KBr) 3010 (m), 1660 (m), 1404 (m), 1168 (s), 1104 (m), 1068 (s), 1001 (m), 960 (s), 945 (m), 770 (m), 762 cm^{-1} (m); ^1H NMR δ 7.34–7.0 (str m, 4 H), 5.89 (s, 4 H), 5.58 (s, 1 H), 4.05 (s, 4 H); mass spectrum, exact mass calcd for $C_{16}H_{13}O_3Br$ m/e 334.0027, obsd m/e 334.0034.

Preparation of 11a. To a solution of **10** (1.5 g, 4.5 mmol) in Et_2O (100 mL) containing a catalytic amount of dichloro[1,3-bis(diphenylphosphino)propane]nickel(II)[12] (20 mg) at 0 °C was added dropwise phenylmagnesium bromide (5.4 mL of a 2.1 M solution in Et_2O); after 5 min, dark crystals of magnesium bromide began to appear on the sides of the flask. After stirring for 1 h at room temperature, TLC analysis (1:1 Et_2O/PE, two elutions) indicated no remaining **10**. The reaction was carefully quenched with sufficient water (2 mL) to coagulate the magnesium salts, the Et_2O/product solution was decanted off, and the magnesium salts were washed with Et_2O (2 × 25 mL). The combined organics were washed with saturated aqueous $NaHCO_3$ (50 mL). The residue after workup was crystallized from Et_2O/PE to afford **11a** (0.735 g, 49%) in two crops as white crystals: mp 168–170 °C dec; IR (KBr) 1650 (m), 1460 (m), 1398 (m), 1115 (s), 1105 (s), 1055 (s), 995 (m), 970 (m), 958 (s), 940 (s), 751 cm^{-1} (m); ^1H NMR δ 7.8–7.0 (str m, 9 H), 6.0 (s, 4 H), 5.98 (s, 1 H), 4.1 (s, 4 H); mass spectrum, exact mass calcd for $C_{22}H_{18}O_3$ m/e 330.1256, obsd m/e 330.1261.

Preparation of 11b–d. The procedure for preparation of these compounds was essentially that used for **11a** except that the product was chromatographed on silica gel before recrystallization from Et_2O in the case of **11b,c**. The data below are listed in the following order: the amounts of **10**; equivalents of Grignard reagent; amount of Et_2O; reaction time; elution solvent; percent yield; melting point; spectroscopic properties.

11b: 0.50 g; 4 equiv; 35 mL; 8 h; 5% Et_2O/PE; 330 mg, 61%; mp 205–206 °C; IR (KBr) 1650 (m), 1605 (m), 1597 (m), 1510 (s), 1460 (m), 1400 (m), 1290 (m), 1245 (s), 1170 (m), 1135 (m), 1115 (m), 1105 (m), 1050 (m), 1020 (m), 960 (s), 940 (m), 840 (m), 750 cm^{-1} (m); ^1H NMR δ 7.0–7.4 (m, 4 H), 7.2 (AB q, $\Delta\nu$ = 56 Hz, J_{AB} = 9 Hz, 4 H), 5.9 (s, 4 H), 5.8 (s, 1 H), 4.0 (s, 4 H), 3.7 (s, 3 H); mass spectrum, exact mass calcd for $C_{23}H_{20}O_4$ m/e 360.1362, m/e obsd 360.1353.

11c: 0.60 g; 3.3 equiv; 10 mL; 0.5 h; 5% Et_2O/PE; 320 mg, 52%; mp 144–145 °C; IR (KBr) 1658 (m), 1510 (m), 1468 (m), 1460 (m), 1405 (m), 1342 (m), 1209 (m), 1210 (m), 1195 (m), 1120 (s), 1105 (s), 1058 (s), 1015 (m), 1000 (m), 960 (s), 945 (m), 830 (m), 760 cm^{-1} (m); ^1H NMR δ 7.2 (AB q, $\Delta\nu$ = 33 Hz, J_{AB} = 8 Hz, 4 H), 7.1–7.4 (m, 4 H), 5.9 (s, 4 H), 5.8 (s, 1 H), 4.0 (s, 4 H), 2.2 (s, 3 H); mass spectrum, exact mass calcd for $C_{23}H_{20}O_3$ m/e 344.1412, obsd m/e 344.1386.

11d: 0.0.48 g; 4 equiv; 20 mL; 2 h; recrystallized from Et_2O/PE; 354 mg, 62%; mp 155–156 °C; IR (KBr) 1650 (m), 1615 (m), 1470 (m), 1410 (m), 1325 (s), 1170 (m), 1115 (s), 1070 (m), 975 (m), 960 (m), 850 (m), 760 cm^{-1} (m); ^1H NMR δ 7.7 (AB q, $\Delta\nu$ = 10 Hz, J_{AB} = 8 Hz, 4 H), 7.1–7.5 (m, 4 H), 6.0 (s, 4 H), 5.9 (s, 1 H), 4.1 (s, 4 H); mass spectrum, exact mass calcd for $C_{23}H_{17}O_3F_3$ m/e 398.1130, obsd m/e 398.1134.

Preparation of 12a. To a solution of **11a** (0.5 g, 1.51 mmol) in THF (20 mL) at 0 °C, chilled 0.1 N HCl (10 mL) was added, and the resulting homogeneous mixture was stored at 0 °C for 12 h. TLC analysis (2:1 PE/Et_2O) indicated some remaining starting material, so the mixture was allowed to warm to room temperature for 4 h, after which time TLC showed the hydrolysis to be complete. The mixture was poured into saturated aqueous $NaHCO_3$ (25 mL), and the resulting precipitate was collected by vacuum filtration and dried in vacuo to afford **12a** (0.414 g, 96%) as a light yellow solid, mp 138–140 °C. Recrystallization of a portion from Et_2O/PE gave the analytical sample as bright yellow crystals: mp 141–142 °C; IR (KBr) 1679 (s), 1630 (m), 1460 (m), 1065 (m), 1055 (m), 960 (s), 868 (m), 758 (s), 690 cm^{-1} (m); ^1H NMR δ 7.8–7.0 (str m, 9 H), 6.5 (AB q, $\Delta\nu$ = 40 Hz, J_{AB} = 10 Hz, 4 H), 6.0 (s, 1 H); mass spectrum, exact mass calcd for $C_{20}H_{14}O_2$ m/e 286.0994, obsd m/e 286.0988.

Preparation of 12b–d. The ketal hydrolyses of **11b–d** were performed similarly to that described for **11a**. For these reactions the following data are given: amount of ketal; amount of THF; amount of HCl; reaction time; purification method; yield; melting point; and spectroscopic properties.

12b: 250 mg; 30 mL; 5 mL of a 0.1 M solution; room temperature for 6 h; chromatographed on silica gel (16 × 1.3 cm column, 5% Et_2O/PE as eluant); 190 mg, 86%; mp 97–98 °C: IR (KBr) 1675 (s), 1630 (m), 1610 (m), 1600 (m), 1510 (s), 1460 (m), 1290 (m), 1250 (s), 1170 (m), 1050 (m), 1020 (m), 960 cm^{-1} (m); ^1H NMR δ 7.6 (d, J = 9 Hz, 2 H), 7.5–6.6 (str m, 8 H), 6.2 (d, J = 10 Hz, 2 H), 5.9 (s, 1 H), 3.7 (s, 3 H); mass spectrum, exact mass calcd for $C_{21}H_{16}O_3$ m/e 316.1099, obsd m/e 316.1116.

12c: 150 mg; 15 mL; 5 mL of a 0.1 M solution; room temperature for 8 h; recrystallized from methanol to obtain a yellow solid: 120 mg, 92%; mp 112–113 °C; IR (KBr) 1680 (s), 1635 (m), 1600 (m), 1520 (m), 1470 (m), 1460 (m), 1390 (m), 1340 (m), 1165 (m), 1065 (m), 1060 (m), 1030 (m), 970 (m), 865 (m), 835 (m), 830 (m), 760 cm^{-1} (m); ^1H NMR δ 7.7–6.9 (str m, 8 H), 6.5 (AB q, $\Delta\nu$ = 30 Hz, J_{AB} = 10 Hz, 4 H), 5.9 (s, 1 H), 2.3 (s, 3 H); mass spectrum, exact mass calcd for $C_{21}H_{16}O_2$ m/e 300.1150, obsd m/e 300.1164.

12d: 180 mg; 20 mL; 5 mL of a 0.1 M solution; room temperature for 6 h; 150 mg, 94%; recrystallized from methanol; 150 mg, 94%; mp 142–144 °C; IR (KBr) 1700 (m), 1675 (s), 1655 (m), 1630 (m), 1610 (m), 1460 (m), 1410 (m), 1320 (s), 1155 (m), 1150 (m), 1115 (s), 1065 (s), 1055 (m), 960 (m), 850 (m), 750 cm^{-1} (m); ^1H NMR δ 7.0–7.8 (m, 8 H), 6.5 (AB q, $\Delta\nu$ = 27 Hz, J_{AB} = 10 Hz, 4 H), 6.0 (s, 1 H); mass spectrum, exact mass calcd for $C_{21}H_{13}O_2F_3$ m/e 354.0868, m/e obsd 354.0894.

Thermal Rearrangement of 12a. A solution of **12a** (0.25 g, 0.87 mmol) in toluene (10 mL) containing 2,6-di-*tert*-butylhydroquinone (2.0 mg) was degassed by three freeze–thaw cycles and heated at reflux for 4 h, after which time TLC analysis (1:1 Et_2O/PE) indicated no remaining starting material and a single, slower moving spot. The reaction mixture was concentrated in vacuo, and the solid residue was triturated with cold Et_2O and dried to afford **13a** (0.207 g, 83%) as light tan crystals, mp 152–155 °C. Recrystallization of a portion from Et_2O/PE gave the analytically pure material: mp 155–157 °C; IR (KBr) 1715 (s), 1670 (s), 1630 (m), 1595 (m), 866 (m), 761 cm^{-1} (m); ^1H NMR δ 7.9–6.9 (highly str m, 9 H), 6.4–6.2 (highly str m, 3 H), 5.8 (dd, J = 10, 1.8 Hz, 1 H), 4.2 (s, 1 H); ^{13}C NMR δ 201.7, 185.1, 151.5, 150.3, 150.0, 135.8, 135.6, 134.0, 129.7, 129.5, 129.0 (2 C), 128.6 (2 C), 128.3 (2 C), 125.6, 125.0, 63.4, 53.4; mass spectrum, exact mass calcd for $C_{20}H_{14}O_2$ m/e 286.0993, obsd m/e 286.0979.

Thermal Rearrangement of 12b–d. These were conducted in sealed tubes in degassed benzene or toluene at 110–130 °C essentially as described for thermal rearrangement of **12a**, and the products were recrystallized from CH_3OH. Only the workup and spectroscopic properties are given.

12b: The ketone (100 mg) gave a crude product, which was recrystallized from Et_2O/PE to give the product as a white solid (81 mg, 81%): mp 131–132 °C; IR (KBr) 1725 (s), 1670 (s), 1625 (m), 1610 (m), 1600 (m), 1515 (s), 1460 (m), 1290 (m), 1250 (s), 1220 (m), 1180 (m), 1030 (m), 870 (m), 850 cm^{-1} (m); ^1H NMR δ 8.0–7.8 (m, 1 H), 7.7–6.7 (m, 8 H), 6.6–6.2 (m, 2 H), 5.9 (dd, J = 10, 1.7 Hz, 1 H), 4.2 (s, 1 H), 3.7 (s, 3 H); mass spectrum, exact mass calcd for $C_{21}H_{16}O_3$ m/e 316.1009, obsd m/e 316.1012.

12c: The ketone (50 mg) gave the product as a white solid (44 mg, 88%): mp 152–153 °C; IR (KBr) 1720 (s), 1670 (s), 1630 (m), 1600 (m), 1515 (m), 1460 (m), 1405 (m), 1300 (m), 1225 (m), 1110 (m), 870 (m), 850 (m), 775 (m), 760 cm^{-1} (m); ^1H NMR δ 8.0–7.8 (m, 1 H), 7.7–7.3 (m, 2 H), 7.2–6.7 (m, 6 H), 6.5–6.1 (m, 2 H), 5.9 (dd, J = 10, 1.7 Hz, 1 H), 4.1 (s, 1 H), 2.2 (s, 3 H); mass spectrum, exact mass calcd for $C_{21}H_{16}O_2$ m/e 300.1150, obsd m/e 300.1153.

12d: The ketone (30 mg) gave a crude product which was chromatographed on silica gel (12 × 1 cm column, 10% Et_2O/PE as eluant), affording a white solid (25 mg, 83%): mp 105–106 °C; IR (KBr) 1725 (s), 1670 (s), 1620 (m), 1600 (m), 1465 (m), 1410 (m), 1330 (s), 1170 (s), 1130 (s), 1070 (s), 1020 (m), 850 (m), 760 cm^{-1} (m); ^1H NMR δ 8.0–7.0 (m, 9 H), 6.6–6.2 (highly str m, 2 H), 5.95 (dd, J = 10, 1.7 Hz, 1 H), 4.3 (s, 1 H); mass spectrum, exact mass calcd for $C_{21}H_{13}O_2F_3$ m/e 354.0868, m/e obsd 354.0859.

Thermal Rearrangement of 9b. A solution of **9b** (0.25 g, 0.93 mmol) in *o*-dichlorobenzene (10 mL) containing 2,6-di-*tert*-butylhydroquinone (2.0 mg) was degassed by three freeze–thaw cycles and heated at reflux under N_2 for 16 h, after which time TLC analysis (1:1 Et_2O/PE) indicated no remaining starting material. The solvent was removed in vacuo, and the residue was chromatographed on silica gel (6 in. × $^1/_2$ in. column, 20% EtOAc/PE as eluant) to afford **14** (0.122 g, 49%) as a clear oil: IR (NaCl) 2970 (m), 2880 (m), 1720 (br, s), 1600 (m), 1462 (m), 1412 (m), 1210 (m), 1100 (br, s), 1030 (m), 1015 (m), 960 (br, s), 925 (m), 750 cm^{-1} (m); ^1H NMR δ 7.8–7.2 (str m, 4 H), 5.95 (br s, 2 H), 5.65 (AB q with additional coupling, $\Delta\nu_{AB}$ = 35 Hz, J_{AB} = 11 Hz, 2 H), 4.0 (s, 4 H), 2.7 (q, J = 7 Hz, 1 H), 1.1 (d, J = 7 Hz, 3 H); ^{13}C NMR δ 205.7, 155.7, 135.3, 135.0, 134.5, 128.4, 127.3, 125.8, 125.7, 123.8, 65.3, 65.1, 53.1, 49.1, 9.8 (two C missing); mass spectrum, exact mass calcd for $C_{17}H_{16}O_3$ m/e 268.1100, obsd m/e 268.1084.

The structural assignment for **14** was further confirmed by hydrolysis of the ethylene glycol ketal moiety as follows. To a solution of **14** (0.018 g, 0.067 mmol) in $(CH_3)_2CO$ (10 mL) was added 5% aqueous HOAc (5 mL), and the mixture was allowed to stand at room temperature for 12 h. Next, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (10 mL), and the solvent was removed in vacuo. Extractive workup using Et_2O (2 × 10 mL) gave **14** (0.015 g, 99%), mp 144–147 °C, with spectral properties identical with those previously described for **6b**.

Details for Kinetic Measurements. A detailed description and representative kinetic and Arhenius plots are given in the supplementary material. The progress for reaction of compounds **5a,b** were determined by removing sealed, degassed ampoules of **5a** (6.3×10^{-2} M) and **5b** (5.8×10^{-2} M) from a constant-temperature bath and analyzing the progress of reaction by ^1H NMR spectroscopy. The NMR analysis for the **5a** reaction was performed by integrating the relative areas of the vinyl protons at δ 4.65 vs the two methylene protons in the product at δ 2.95. For **5b** the allylic methyl resonance at δ 1.8 was integrated vs the ketone methyl resonance at δ 1.2. For the aryl substituted compounds, **12a–d**, a similar sealed tube technique was employed, except the disappearance of starting material was analyzed by UV. These concentrations for the kinetic runs were (6.7–7.7) × 10^{-4} M and the analyses performed at the indicated wavelengths: **12a** (346.5 nm); **12b** (355 nm); **12c** (350 nm); **12d** (349.5 nm) on solutions diluted so that the maximum optical density was <1.0. The kinetic determinations employing ^1H NMR spectroscopy are thought to be accurate to at least ±10% while those determined employing UV spectroscopy are probably accurate to at least ±5%.

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Supplementary Material Available: Detailed description of the kinetic procedures, ^1H NMR spectra of **5a, 6a, 6b, 11a, 12a,** and **13a**, and representative kinetic and Arhenius plots (12 pages). Ordering information is given on any current masthead page.

The Baconipyrones: Novel Polypropionates from the Pulmonate *Siphonaria baconi*

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The pulmonate mollusc *Siphonaria baconi* from the south coast of Australia contains four new propionate-derived metabolites, baconipyrones A–D (**5–8**), in addition to the known compound siphonarin A (**3**). The structure of baconipyrone B (**6**) was determined by X-ray analysis. The structures of baconipyrones A (**5**), C (**7**), and D (**8**) were established by comparison of spectral data with those of baconipyrone B (**6**) and by consideration of a biosynthetic hypothesis linking the baconipyrones with the siphonarins.

The Siphonariids, or false limpets, are pulmonate molluscs that live in the intertidal zone. They possess both a gill and a primitive lung that enables them to "breathe" both above and under water. From the chemists' viewpoint, they are characterized by their ability to synthesize compounds of the polypropionate class.[1] The metabolites described previously[2] all fall into three general classes: the simple polypropionates, such as denticulatin A (**1**) from *Siphonaria denticulata*,[3] the α-pyrones, exemplified by diemenensin (**2**) from *S. diemenensis*,[4] and γ-pyrones like siphonarins A (**3**) and B (**4**) from *S. zelandica* and *S. atra*.[5] In this paper we describe four new polypropionates, baconipyrones A–D (**5–8**), that are unusual[6] because they do not contain a contiguous carbon skeleton.

Specimens of *Siphonaria baconi* were collected from intertidal rock platforms near Melbourne, Australia, and were stored in acetone. The ethyl acetate soluble material from the acetone extract was chromatographed on silica gel, and fractions containing polypropionates, as judged by ^1H NMR spectroscopy, were further purified by HPLC to obtain baconipyrone A (**5**, 0.05 mg/animal), baconipyrone B (**6**, 0.046 mg/animal), baconipyrone C (**7**, 0.016 mg/animal), baconipyrone D (**8**, 0.046 mg/animal), and

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