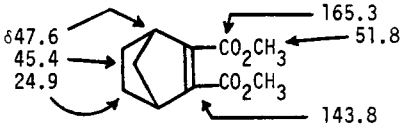
pheric pressure under an atmosphere of hydrogen until 1.1 L had been consumed. GLC analysis of the reaction mixture revealed the presence of **5** along with a small amount of the completely reduced diester (endo-**6**). The suspension was filtered and concentrated (rotary evaporator), and the crude product (8.86 g) was distilled under reduced pressure, giving 7.85 g (84%) of a colorless oil, **5**: bp 118 °C (6–8 mmHg) [lit.[29] bp 132–133 °C (12 mmHg)]; ^{1}H NMR ($CDCl_3$) δ 3.77 (s, 6 H, CO_2CH_3), 3.30 (br s, 2 H, $CHCH_2CH$), 2.10–1.10 (m, 6 H, $CH_2CHCH_2CHCH_2$).

The ^{13}C NMR spectrum of diester **5** is shown below, and the assignments are consistent with the off-resonance coupling spectrum.



1,3-Cyclohexadiene (2). A neat solution of *trans*-1,2-dibromocyclohexane (61.9 g, 0.26 mol) was added dropwise to a mechanically stirred suspension of sodium hydroxide pellets (31.6 g, 0.79 mol) in 2-methoxyethanol (69.0 g, 1.13 mol) heated to ca 125 °C, allowing for the concurrent distillation of a water–crude product mixture. The distilling head temperature was maintained below 100 °C, and the distillation continued for 0.5 h after the addition was completed. The two components of the distillate were separated, and the organic layer was dried ($CaCl_2$) and distilled to afford **2**: 1.5 mL (44.6%); bp 79–80 °C (lit.[30] bp 78–88 °C); ^{1}H NMR ($CDCl_3$) δ 5.68 (s, 4 H, CH=CH), 2.05 (s, 4 H, ring CH_2).

1-Methylcyclohexene (12). 1-Methyl-1-hydroxycyclohexane (90.0 g, 0.81 mol) was prepared from the reaction of cyclohexanone (125 g, 1.27 mol) and methylmagnesium iodide [prepared from magnesium turnings (31.0 g, 1.29 mmol) and methyl iodide (183 g, 1.29 mol)]. The 1-methyl-1-hydroxycyclohexanone was added dropwise to a solution of concentrated phosphoric acid (35 mL), preheated to approximately 110–120 °C, allowing for the olefin–water mixture to distill into a cooled receiver (ice bath) at 5 °C. The crude product was decanted from water, dried ($MgSO_4$), and distilled over sodium to give 80 g (91%) of **12**, bp 105–107 °C (lit.[31] bp 108–109 °C). GLC analysis showed a product of 96% purity (the external olefin was the only other component).

1-Methyl-4-*tert*-butylcyclohexene (13). A solution of 4-*tert*-butylcyclohexanone (23.0 g, 0.149 mol) in anhydrous diethyl ether (100 mL) was added dropwise at 5 °C with stirring to methylmagnesium iodide, prepared by the addition of iodomethane (23.2 g, 0.164 mol) in dry ether (50 mL) to a suspension of magnesium turnings (3.93 g, 0.164 atom) in dry ether (50 mL). The suspension containing the ketone and Grignard reagent was heated (steam bath) for 2 h. The suspension was cooled to 5 °C (ice bath) and treated with 1.6 M hydrochloric acid (120 mL). The suspension was further heated as necessary to completely dissolve any unreacted magnesium. The solution was again cooled and the ethereal layer collected. The aqueous layer was extracted with ether (2 × 250 mL), and the ethereal layers were combined. The ethereal solution was treated with solid sodium bicarbonate until neutral, dried ($MgSO_4$), and concentrated (steam bath) to a dark yellow liquid which solidified upon standing. The solid was dissolved in a solution of benzene containing *p*-toluenesulfonic acid (1 g) and the mixture refluxed, allowing for the water to be collected in a Dean–Stark trap. After 2.6 mL of water had been collected, the mixture was cooled (ice bath), neutralized with solid sodium bicarbonate, dried ($CaCl_2$), and concentrated by distillation to give the crude product (15.9 g, 71%) in greater than 95% purity by GLC analysis. Distillation from sodium afforded the colorless product **13**: 11.0 g (49%); bp 77–78 °C (16 mmHg) [lit.[32] bp 53 °C (2.5 mmHg), greater than 99% purity by GLC analysis]; ^{1}H NMR ($CDCl_3$) δ 5.37 (s, 1 H, $CH=C(CH_3)$, 1.05–2.50 [m, 10H, $(CH_2)CHC(CH_3)$], 0.85 [s, 9 H, $-CH(CH_3)_3$].

1-Methyl-4-isopropylcyclohexene (14). A suspension of 10% platinum on carbon (0.40 g) in freshly distilled *d*-limonene (71.4 g, 0.524 mol) was treated with hydrogen gas at an initial pressure of 60 lb/sq in. The reaction was terminated after a pressure drop of 43.5 lb/sq in. had been recorded. The catalyst was removed by suction filtration, and colorless liquid distilled over sodium to afford 65 g (90%) of **14**, bp 77–77.5 °C (31 mmHg) [lit.[18] bp 77.5–78 °C (35 mmHg)].

Acknowledgement is made to the North Carolina Science and Technology Committee and the University of North Carolina's Research Council for financial support of this work. We also thank Dr. David L. Harris for recording numerous ^{1}H and ^{13}C NMR spectra related to this work. We are especially grateful to Professor Samuel Siegel of the University of Arkansas for his valuable suggestions and comments.

Registry No. 1, 110-83-8; 2, 592-57-4; 3, 947-57-9; *endo*-4, 39589-98-5; 5, 17931-56-5; *endo*-6, 4098-47-9; 7, 119-64-2; 8, 5989-27-5; 9, 4221-98-1; 10, 99-86-5; 12, 591-49-1; 13, 3419-74-7; 14, 5502-88-5; Pd, 7440-05-3; cyclopentadiene, 542-92-7; dimethyl acetylenedicarboxylate, 762-42-5; *trans*-1,2-dibromocyclohexane, 7429-37-0; 1-methyl-1-hydroxycyclohexane, 590-67-0; cyclohexanone, 108-94-1; methyl iodide, 74-88-4; 4-*tert*-butylcyclohexanone, 98-53-3; 4-*tert*-butyl-1-methylcyclohexanol, 6353-54-4.

(29) Diels, O.; Alder, K. *Justus Leibigs Ann. Chem.* **1931**, *490*, 240.
(30) Schaefer, J. P.; Endres, P. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 285.
(31) Huntsman, W. D. *J. Am. Chem. Soc.* **1960**, *82*, 6389.
(32) Bordwell, F. G.; Landis, P. S.; Whitney, G. S. *J. Org. Chem.* **1965**, *30*, 3764.

Enones with Strained Double Bonds. 8. The Bicyclo[3.2.1]octane Systems[1]

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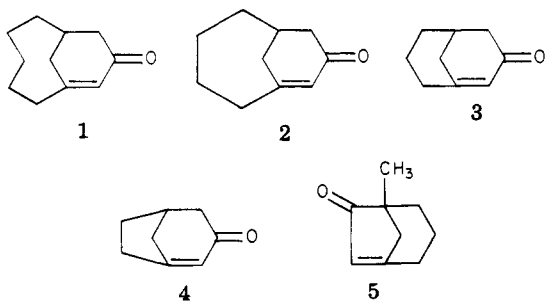
The bicyclic enones bicyclo[3.2.1]oct-1-en-3-one (**4**) and 1-methylbicyclo[3.2.1]oct-5(6)-en-7-one (**5**) have been generated from various precursors and trapped by the addition of nucleophiles such as MeOH, PhSeH, or H_2O. The bridgehead enone **5** has also been trapped as its cycloadduct **31** with furan. Pyrolysis of this cycloadduct **31** reformed the bridgehead enone **5** that was trapped as the cycloadduct **32**. Related bridgehead enones **35** and **47** have also been generated as intermediates leading to products with bridgehead methoxy substituents.

Our earlier studies of enones with bridgehead double bonds have included the bicyclo[5.3.1]undecane **1**,[2] the bicyclo[4.3.1]decane **2**,[3] and the bicyclo[3.3.1]nonane **3**.[4] Since the variety and degree of reactivity observed for

0022-3263/83/1948-1643$01.50/0

Chart I



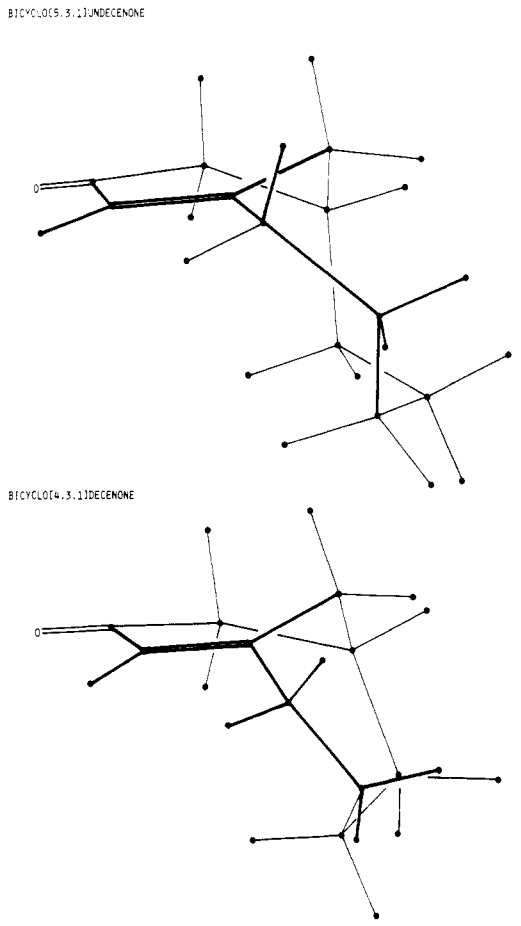


Figure 1. Perspective views of bicyclo[5.3.1]undecenone and bicyclo[4.3.1]decenone.

these enones increased with the lower (and more highly distorted) homologues, we were led to explore representatives of the next lower homologue, the bicyclo[3.2.1]octane system. In this paper, reaction sequences are described that lead to the transient formation of the bicyclic enones **4** and **5** (Chart I).

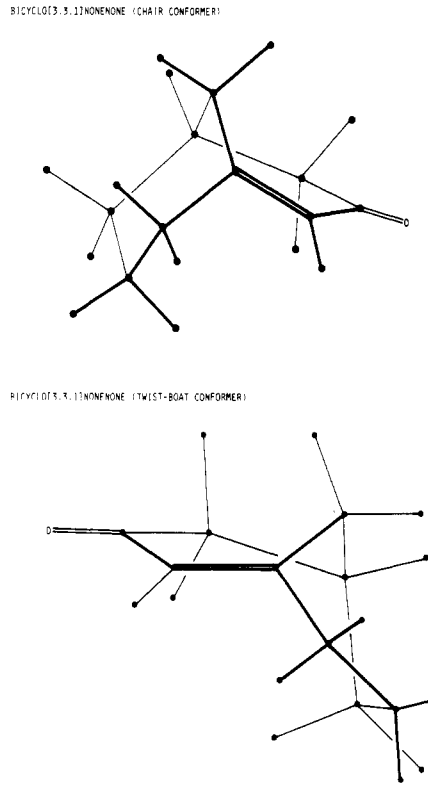


Figure 2. Perspective views of the twist-boat and chair conformers of bicyclo[3.3.1]nonenone.

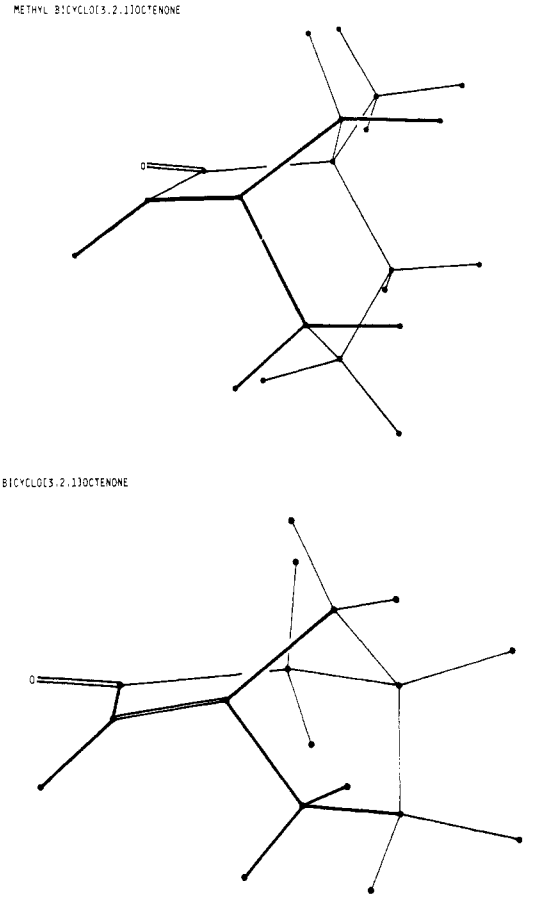


Figure 3. Perspective view of bicyclo[3.2.1]octenone and methylbicyclo[3.2.1]octenone.

Estimates of the probable geometry and the extent of strain in each of these enones **1–5** were obtained from molecular mechanics calculations employing Allinger's

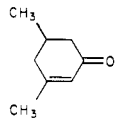
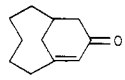
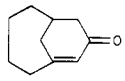
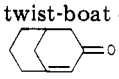
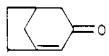
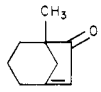
(1) A portion of this research has been supported by Public Health Service Grant R01-GM-30735 from the National Institute of General Medical Science. The execution of this research was also aided by Institutional Research Grants from the National Science Foundation for the purchase of a mass spectrometer and an NMR spectrometer.

(2) (a) House, H. O.; Sieloff, R. F.; Lee, T. V.; DeTar, M. B. *J. Org. Chem.* **1980**, *45*, 1800. (b) House, H. O.; Sieloff, R. F.; VanDerveer, D. *Ibid.* **1981**, *46*, 4639.

(3) House, H. O.; Lee, T. V. *J. Org. Chem.* **1979**, *44*, 2819.

(4) (a) House, H. O.; DeTar, M. B.; VanDerveer, D. *J. Org. Chem.* **1979**, *44*, 3793. (b) House, H. O.; DeTar, M. B.; Sieloff, R. F.; VanDerveer, D. *Ibid.* **1980**, *45*, 3545. (c) A preliminary report, published after this manuscript was submitted, describes the transient generation of several bicyclo[3.3.1]enones and bicyclo[3.2.1]enones in ethanol solution. See: Bestmann, H. J.; Schade, G. *Tetrahedron Lett.* **1982**, *23*, 3543.

Table I. Calculated C=C Deformations and Strain Energies

compound	average twisting deformation, deg	pyramidal deformations, deg	C=C deformation kcal/mol	inherent strain, kcal/mol
	2.5	2 and 4	0.2	3.4
	4	1 and 9	0.5	16.9
	14	14 and 21	4.7	17.7
twist-boat conformer of 	21	19 and 37	11.3	21.3
(chair conformer)	(25)	(25 and 42)	(16.5)	(20.8)
	36	29 and 60	30.5	32.3
	36	36 and 62	32.8	27.4

MMP1 program for conjugated systems.[5] Perspective drawings of the conformations of these molecules obtained after energy minimization are presented in Figures 1–3. The inherent strain values obtained from these force field calculations are summarized in Table I along with estimates of the amount of strain resulting from deformation of the C=C bond. These latter estimates of C=C deformation are obtained by the method of Ermer,[6,7] employing the average C=C twisting deformation and the pyramidal deformations at each end of the C—C double bond. The angular values for the twisting and pyramidal deformations (listed in Table I) were obtained from the force field calculations.

Both bicyclo[3.2.1]octenones **4** and **5** are estimated to have considerably more distortion and strain than the bicyclo[3.3.1]nonenone **3**. In view of our difficulties in seeking to isolate the bicyclo[3.3.1]system,[4] we are led to expect that isolation of the bicyclo[3.2.1]systems **4** and **5** will require unusual conditions. However, the generation of the enones **4** and **5** as transient intermediates appeared to be a reasonable goal.

Our synthetic approach to the bicyclic enone **4** is related to the earlier observation that an intramolecular application of the Wittig olefin synthesis is capable of forming bridgehead olefinic double bonds.[8] As illustrated in Scheme I, the diketo phosphonate **12** was generated in several steps from the lactone **8**;[9] in this case direct reaction of the lactone **8** with the lithio phosphonate **11** gave poor yields. Reaction of this diketo phosphonate **12** with NaH in the aprotic solvent DME formed, after neutralization, the hydroxy phosphonate **13** that failed to eliminate in the aprotic reaction mixture. However, either treatment of the phosphonate **13** with base in MeOH or reaction of the phosphonate **12** with base in H_2O or MeOH resulted in generation of the enone **4** that was trapped as the methyl ether **14**, the keto selenide **15**, or the transiently stable ketol **16**. This ketol **16** underwent a reverse aldol reaction to form the diketone **17**. Thus far, we have not found satisfactory methods for regenerating the enone **4** from one of these adducts, **14**, **15**, or **17**.

As illustrated in Scheme II, two methods were employed to obtain precursors **26** for the bicyclic enone **5**. One method, developed previously to form bicyclic ketols,[10] involved reaction of the lactone **20** with lithiomethyl methyl sulfone followed by oxidation to form the diketo sulfone **21**. Subsequent aldol condensation followed by reductive cleavage of the keto sulfone **22** afforded the ketol **23a**. A shorter synthesis utilized reaction of the lactone **20** with the lithio phosphonate **11** followed by oxidation to form the diketo phosphonate **24**. Reaction of this phosphonate **24** with base in a protic solvent generated the bicyclic enone **5** that was trapped with MeOH to form the keto ether **25** or with H_2O to form the ketol **23a**. Reaction of the ketol **23a** with the appropriate sulfonyl chloride formed the two sulfonate esters **26**. As had been noted previously with diketo phosphonate **12**, reaction of the diketo phosphonate **24** with NaH in the aprotic solvent DME formed the aldol intermediate **27** that failed to eliminate in an aprotic medium.

Each of the sulfonate esters **26** underwent elimination when heated with Et_3N in refluxing MeOH or THF (see Scheme III). The initial precipitate formed in these mixtures had spectral properties which suggested that it may be a mixture of a triethylammonium sulfonate and the salt **29**. In any case the salt **29**, if present, was slowly reconverted to the enone **5** in the boiling reaction mixture. The enone **5** was trapped either as the keto ether **25** or as the furan adducts **31**. When the methanesulfonate ester **26a** was employed in these reactions, a byproduct, the disulfonate **28**, was formed. We suggest that this byproduct arises by reaction of the sulfonate **26a** with Et_3N to form the reactive intermediate sulfene **30** that reacts with

(5) For a review, see: Allinger, N. L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1. We are indebted to Professor Allinger and his associates and to the University of Georgia Computer Center for allowing us to use the current versions of the MM2 and MMP1 programs for these calculations.

(6) Ermer, O. *Z. Naturforsch., B: Anorg. Chem., Org. Chem.* **1977**, *32B*, 837.

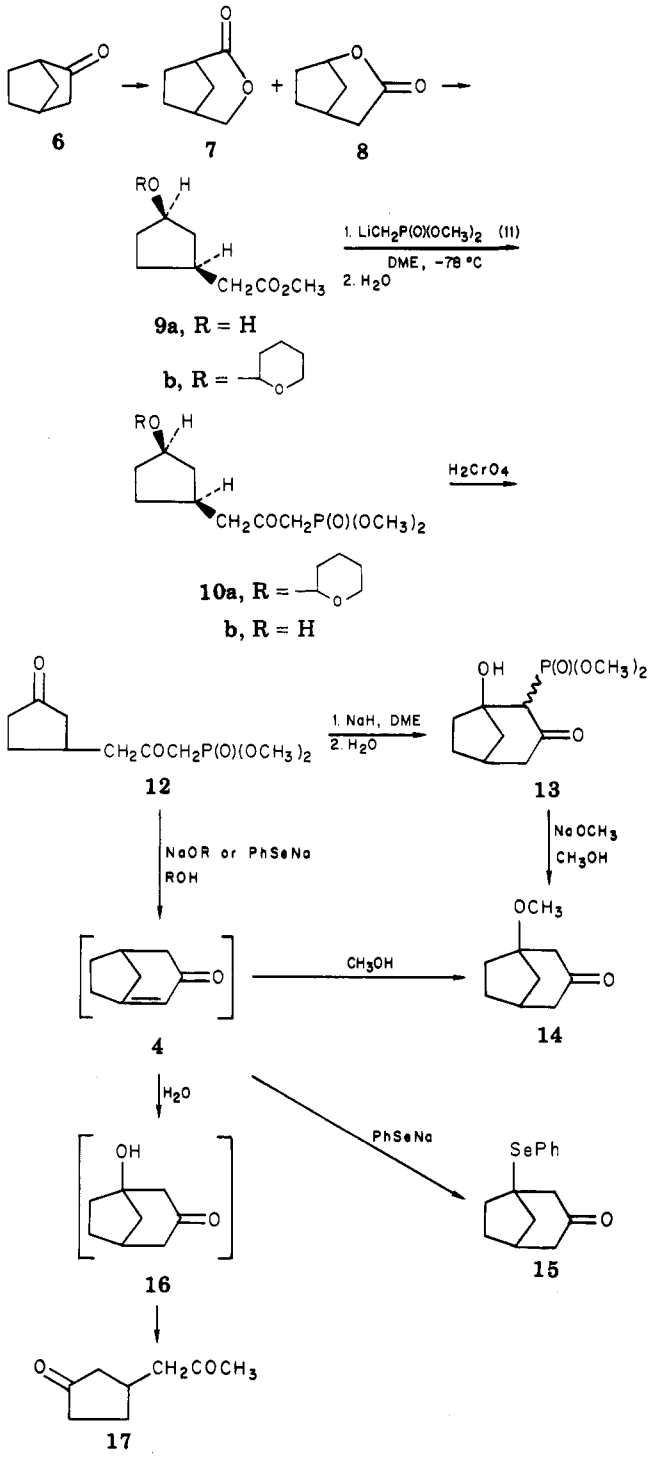
(7) For review and discussion of this and related computation procedures, see: (a) Shea, K. J. *Tetrahedron* **1980**, *36*, 1683–1715. (b) Maier, W. F.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1981**, *103*, 1891.

(8) For a recent review, see: Becker, K. B. *Tetrahedron* **1980**, *36*, 1717.

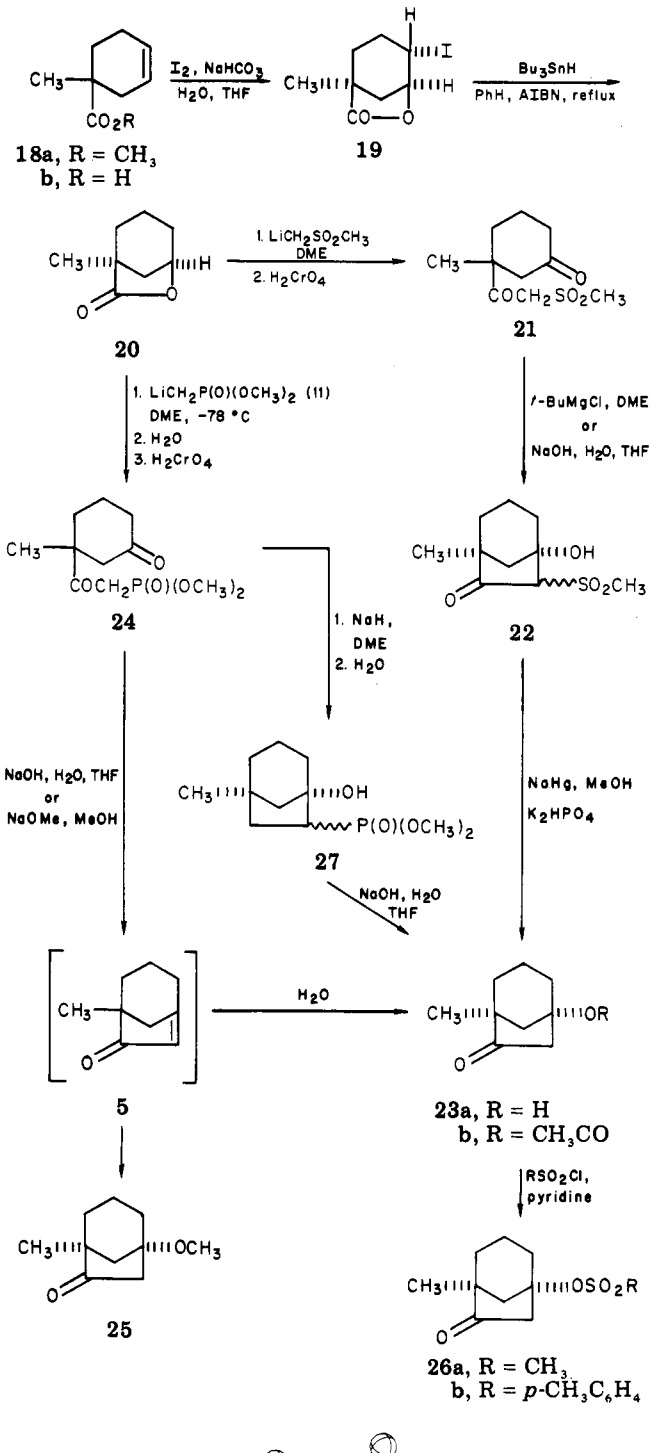
(9) For a similar formation of a keto phosphonate, see: Aristoff, P. *J. Org. Chem.* **1981**, *46*, 1954.

(10) (a) House, H. O.; Melillo, D. G.; Sauter, F. J. *J. Org. Chem.* **1973**, *38*, 741. (b) House, H. O.; Melillo, D. G. *Ibid.* **1973**, *38*, 1398.

Scheme I



Scheme II



the enol form of keto sulfonate **26a**. In accord with this idea, no byproduct analogous to the disulfonate **28** was observed when the keto tosylate **26b** was the precursor for enone **5**. The major stereoisomer **31a** of the furan adduct **31** was separated, and its structure was established by X-ray crystallography (see Figure 4).

Earlier study with the bicyclo[3.3.1]enone **3**[4] suggested that bicyclic enone **5** might be generated by pyrolysis of its furan adduct **31**. Although we have not yet performed appropriate pyrolyses in the gas phase, experiments conducted in a sealed tube suggest that this pyrolytic method has promise. The major product formed in the sealed tube reaction was the adduct **32** formed by cycloaddition of the enone **5** to the starting furan adduct **31** (see Scheme IV). The structure of the adduct was established by X-ray

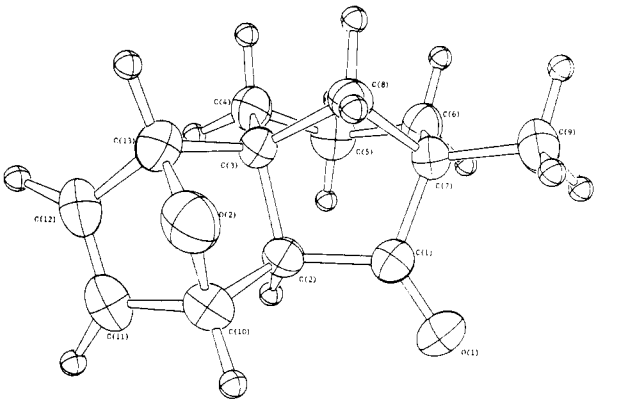
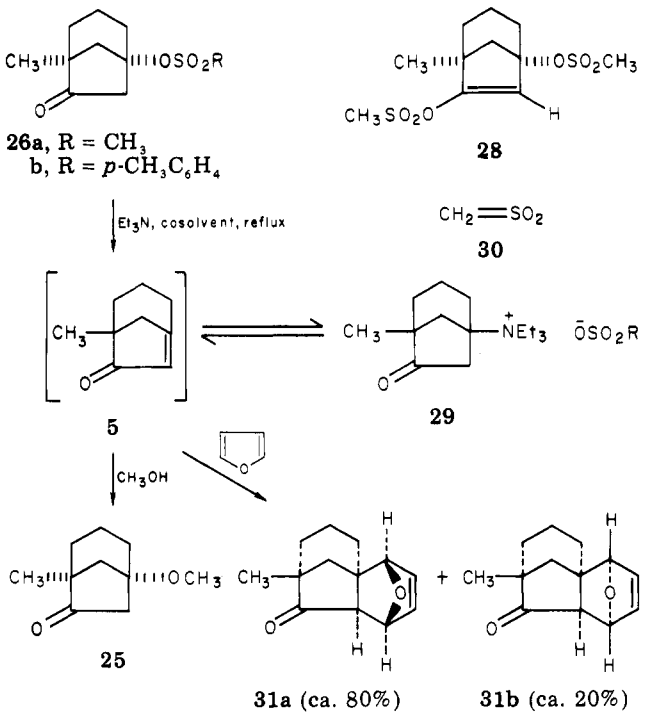


Figure 4. Perspective view of the molecular structure of the adduct from furan and 1-methylbicyclo[3.2.1]oct-5-en-7-one.

Scheme III



Scheme IV

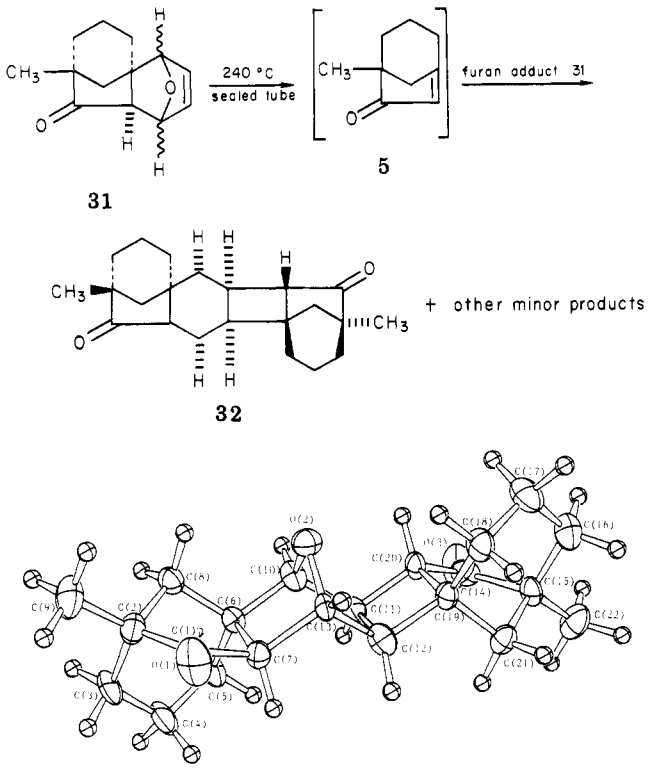
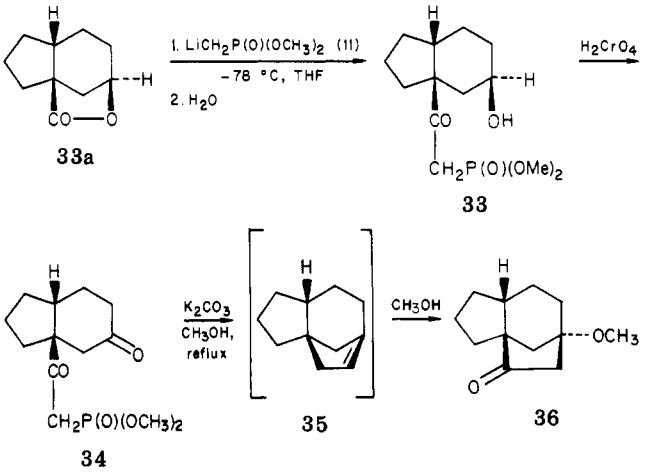


Figure 5. Perspective view of the molecular structure of the adduct **32** formed from the furan adduct **31** and 1-methylbicyclo[3.2.1]oct-5-en-7-one.

crystallography as illustrated in Figure 5. Preliminary experiments that involved heating mixtures of the furan adduct **31** and butadiene in a sealed tube were less promising. The furan adduct **31** apparently formed an adduct with butadiene more rapidly than it underwent a retro-Diels–Alder reaction.

The methodology used to convert the lactone **20** to the methoxy ketone **25** (Scheme II) was also explored briefly with perhydroindan lactone **33a**[11] (see Scheme V) and then

Scheme V



applied to the lactone **44** (see Scheme VI), an intermediate in a proposed gibberellin synthesis.[12] As illustrated in Scheme VI, this methodology involving a bridgehead enone intermediate **47** offers an attractive route to bicyclo[3.2.1]octane derivative **48** with a bridgehead methoxy substituent.

Experimental Section[13]

Preparation of Lactone 8. To a cold (0–5 °C) mixture of 40.0 g (0.23 mol) of *m*-chloroperbenzoic acid, 18.68 g (0.22 mol) of $NaHCO_3$, and 300 mL of CH_2Cl_2 was added, dropwise and with stirring during 30 min, a solution of 22.83 g (0.21 mol) of norcamphor (**6**) in 75 mL of CH_2Cl_2. After the resulting suspension had been stirred at 25 °C for 5 h, it was filtered with suction, and the residue was washed with CH_2Cl_2. The combined filtrates were washed successively with aqueous $NaHCO_3$ and with aqueous NaCl and then dried and concentrated. The residual yellow liquid (22.79 g or 86%) contained (NMR analysis) a mixture of 92% of lactone **8** and 8% of lactone **7**.[14] A solution of this lactone mixture in $CHCl_3$ was washed with two portions of aqueous 1 M NaOH and then washed with aqueous NaCl, dried, and concentrated. The residual colorless semisolid (19.92 g or 72% yield) contained (NMR analysis) the lactone **8**. Sublimation (50–55 °C at 0.05 mm) afforded the pure lactone **8** as colorless waxy crystals: mp 58–59.5 °C (lit.[15] mp 56–58 °C); IR (CCl_4) 1743 cm^{-1} (lactone C=O); ^1H NMR (CCl_4) δ 4.75 (1 H, br, CHOCOR), 1.2–2.9 (9 H, m, aliphatic CH); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 169.8 (s), 85.6 (d), 50.4 (t), 35.6 (t), 32.3 (t), 31.1 (d), 29.0 ppm (t); mass spectrum, *m/e* (rel intensity) 126 (M^+, 29), 98 (37), 83 (97), 82 (100), 70 (39), 69 (70), 67 (90), 56 (38), 55 (78), 54 (62), 44 (30), 43 (58), 42 (78), 41 (55).

(11) House, H. O.; Boots, S. G.; Jones, V. K. *J. Org. Chem.* **1965**, *30*, 2519.

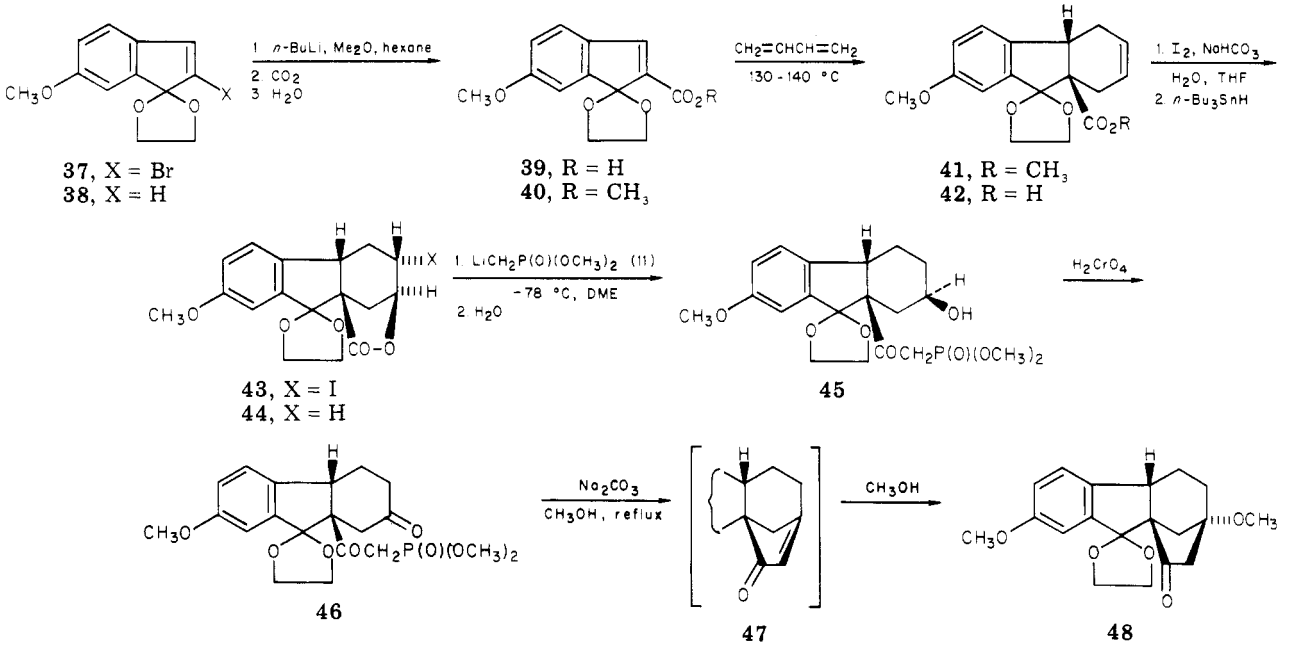
(12) See: House, H. O.; McDaniel, W. C. *J. Org. Chem.* **1977**, *42*, 2155 and references cited therein.

(13) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated $MgSO_4$ was employed as a drying agent. The IR spectra were determined with a Perkin-Elmer Model 299 infrared recording spectrophotometer fitted with a grating. The UV spectra were determined with a Cary Model 14 or a Perkin-Elmer Model 202 recording spectrophotometer. The ^1H NMR spectra were determined at 60 MHz with a Varian Model T-60A NMR spectrometer or at 300 MHz with a Bruker Model WM-300 NMR spectrometer. The ^{13}C NMR spectra were determined at 25 MHz with a JEOL Model PFT-100 NMR spectrometer or at 75 MHz with a Bruker Model WM-300 NMR spectrometer. The chemical shift values are expressed in δ values (ppm) relative to a Me_4Si internal standard. The mass spectra were obtained with either a Hitachi Perkin-Elmer Model RMU-7 or a Varian MAT Model 112S mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

(14) For a recent review of this reaction and related reactions, see: Krow, G. R. *Tetrahedron* **1981**, *37*, 2697.

(15) Meinwald, J.; Frauenglass, E. *J. Am. Chem. Soc.* **1960**, *82*, 5235.

Scheme VI



Preparation of Methyl Esters 9. A solution of 6.65 g (52.8 mmol) of the lactone **8** and 3 mL of aqueous 12 M HCl in 300 mL of MeOH was refluxed for 1 h and then cooled and concentrated. The residual liquid was partitioned between Et_2O and H_2O, and the organic phase was washed with aqueous NaCl, dried, and concentrated. Distillation of the residual yellow liquid separated 7.50 g (90%) of the hydroxy ester **9a** as a colorless liquid: bp 77–79 °C (0.01–0.02 mm); n^{25}_D 1.4609 [lit.[16] bp 92–94 °C (1 mm)]; IR (CCl_4) 3620, 3440 (OH), 1740 cm^{-2} (ester C=O); ^1H NMR (CCl_4) δ 4.0–4.4 (1 H, m, CHO), 3.79 (s, H, exchanges with D_2O, OH), 3.60 (3 H, s, OCH_3), 1.0–2.6 (9 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 158 (M^+, 0.2), 115 (25), 83 (24), 74 (100), 67 (62), 59 (27), 55 (31), 43 (48), 41 (32), and 39 (21).

A mixture of 10.45 g (66.1 mmol) of the hydroxy ester **9a**, 8.10 g (96 mmol) of dihydropyran, and 0.5 mL of aqueous 12 M HCl was stirred at 25 °C for 12 h, and then partitioned between Et_2O and aqueous $NaHCO_3$. The organic layer was washed with aqueous NaCl and then dried, concentrated, and distilled twice in a short-path still (105–107 °C and 0.7 mm) to separate 14.50 g (91%) of the ester **9b** as a colorless liquid: n^{25}_D 1.4650 [lit.[16] bp 72–74 °C (0.2 mm)]; IR (CCl_4) 1740 cm^{-1} (ester C=O); ^1H NMR (CCl_4) δ 3.2–4.9 (7 H, m, OCH including a CH_3O singlet at 3.62) and 1.0–2.6 (15 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 242 (M^+, 6), 141 (82), 109 (57), 101 (45), 85 (100), 84 (64), 83 (45), 82 (53), 81 (73), 69 (44), 67 (73), 57 (57), 56 (53), 55 (81), 54 (49), 43 (62), 42 (40), 41 (86), 39 (69).

Preparation of Diketo Phosphonate 12. Since initial attempts to prepare keto phosphonate **10b** by reaction of the phosphonate anion **11** with the lactone **8** or with the hydroxy ester **9a** were not satisfactory, the following procedure[17] was followed. To a cold (−78 °C) solution of 11.0 g (88.7 mmol) of $CH_3P(O)(OCH_3)_2$ in 100 mL of DME was added, dropwise and with stirring during 30 min, 61 mL of a hexane solution containing 88.7 mmol of *n*-BuLi. After the resulting cold suspension had been stirred for 30 min, a solution of 14.31 g (59.1 mmol) of the methyl ester **9b** in 100 mL of DME was added, dropwise and with stirring during 30 min. The resulting cold (−78 °C) mixture was stirred for an additional 30 min, and then the cooling bath was removed and stirring was continued for 3 h. The resulting mixture was partitioned between $CHCl_3$ and dilute aqueous HCl. The organic layer was washed with aqueous NaCl, dried, and concentrated to leave the crude keto phosphonate **10a** as a pale yellow liquid. A solution of this crude ether **10a** and 500 mg of *p*-TsOH in 100 mL of H_2O and 100 mL of THF was refluxed for 3 h and then concentrated and partitioned between H_2O and Et_2O. Several minor byproducts were present in the Et_2O phase. The aqueous phase was extracted repeatedly with $CHCl_3$, and then the $CHCl_3$ extract was washed with aqueous NaCl, dried, and concentrated. The crude hydroxy keto phosphonate **10b** remained as a pale yellow liquid; IR (CCl_4) 3480 (OH), 1705 cm^{-1} (C=O).

A cold (0–5 °C) solution of 804 mg (3.2 mmol) of the crude hydroxy keto phosphonate **10b** in 50 mL of acetone was treated with 1.1 mL (1.4 equiv) of aqueous 8 N H_2CrO_4. After the reaction mixture had been stirred for 10 min, it was partitioned between $CHCl_3$ and H_2O. The organic layer was washed with aqueous NaCl, dried, and concentrated to leave 797 mg of yellow liquid. Chromatography on silica with first Et_2O and then EtOAc as the eluent separated 678 mg (85%) of the crude liquid diketo phosphonate **12**. Distillation in a short-path still (118–125 °C and 0.01 mm) separated the pure phosphonate **12** as a colorless liquid: n^{25}_D 1.4721; IR (CCl_4) 1745 (cyclopentanone C=O), 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 3.70 (6 H, d, J = 12 Hz, $POCH_3$), 1.2–3.3 (11 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 248 (M^+, <0.1), 167 (24), 166 (26), 151 (42), 124 (100), 109 (67), 94 (75), 79 (45), 55 (20), 41 (30), 29 (21).

Anal. Calcd for $C_{10}H_{17}O_5P$: C, 48.38; H, 6.92. Found: C, 48.38; H, 7.19.

Reaction of Diketo Phosphonate 12 with Bases. A. With NaOMe. A solution of 667 mg (2.7 mmol) of the phosphonate **12** and 5.9 mmol of NaOMe in 16.4 mL of MeOH was refluxed for 1 h and then partitioned between H_2O and $CHCl_3$. The organic phase was washed with aqueous NaCl and then dried and concentrated. The residual pale yellow liquid was chromatographed on silica gel with Et_2O as the eluent to separate 370 mg (90%) of early fractions containing the ketone **14** as a pale yellow liquid. A pentane solution of the ketone **14** was dried over silica gel and then distilled in a short-path still (65–68 °C and 0.9 mm) to separate the pure methoxy ketone **14** as a colorless liquid: n^{25}_D 1.4828; IR (CCl_4) 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 3.22 (3 H, s, OCH_3), 1.2–2.7 (11 H, m, aliphatic CH); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 208.8 (s), 82.8 (s), 52.9 (t), 51.3 (q), 48.7 (t), 40.8 (t), 32.7 (t), 32.0 (d), 28.0 ppm (t); mass spectrum, *m/e* (rel intensity) 154 (M^+, 1.5), 125 (18), 98 (21), 97 (100), 96 (12), 41 (12).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15; M_r, 154.0990. Found: C, 69.81; H, 9.18; M_r, 154.1010 (mass spectrum).

B. With NaOH. A solution of 790 mg (3.2 mmol) of the phosphonate **12** and 6.4 mmol of NaOH in 16.4 mL of H_2O and 10 mL of THF was refluxed for 2.5 h and then concentrated and partitioned between H_2O and $CHCl_3$. After the organic layer had been washed with aqueous NaCl, dried, and concentrated,

(16) Barraclough, P.; Young, D. W. *J. Chem. Soc., Perkin Trans. 1* **1976**, 264.

(17) For a similar procedure, see: Aristoff, P. *J. Org. Chem.* **1981**, *46*, 1954.

chromatography of the residual yellow liquid on silica gel with an Et_2O eluent separated 290 mg (73%) of the diketone **17** in early fractions. None of the aldol product **16** was observed. Two successive distillations in a short-path still afforded the diketone **17** as a colorless liquid: bp 110–112 °C (1.1 mm); n^{25}_D 1.4658; IR (CCl_4) 1740 (cyclopentanone C=O), 1715 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.2–2.7 (m, aliphatic CH including a CH_3CO singlet at 2.10); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 217.6 (s), 206.2 (s), 48.7 (t), 44.4 (t), 38.0 (t), 32.1 (d), 30.1 (q), 29.1 ppm (t); mass spectrum, *m/e* (rel intensity) 140 (M^+, 0.2), 83 (43), 82 (43), 55 (15), 43 (100), 41 (18), 39 (14).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63; M_r, 140.0834. Found: C, 68.52; H, 8.70; M_r, 140.0829 (mass spectrum).

C. With NaH. To a suspension of 95 mg (3.9 mmol) of powdered NaH (previously washed with hexane) in 10 mL of DME was added, dropwise and with stirring during 5 min, a solution of 427 mg (1.7 mmol) of the phosphonate **12** in 10 mL of DME. The resulting suspension was stirred at 25 °C for 1 h and then partitioned between $CHCl_3$ and cold aqueous 1 M HCl. The organic layer was washed with aqueous NaCl, dried, and concentrated to leave a yellow liquid. Chromatography on silica gel with an EtOAc eluent separated 325 mg (76%) of the keto phosphonate **13** in late fractions. This material was distilled in a short-path still (156–161 °C and 0.1–0.3 mm) to afford the keto phosphonate **13** as a colorless liquid: n^{25}_D 1.4738; IR (CCl_4) 3450 (br, OH), 1710 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 3.73 (6 H, d, J = 12 Hz, $POCH_3$), 1.2–3.4 (11 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 248 (M^+, 1.3), 219 (18), 191 (14), 127 (100), 109 (15), 80 (21), 79 (36), 41 (14).

Anal. Calcd for $C_{10}H_{17}O_5P$: C, 48.36; H, 6.92; M_r, 248.0809. Found: C, 48.49; H, 7.37; M_r, 248.0815 (mass spectrum).

When a solution of the diketo phosphonate **12** and NaOH in aqueous THF was stirred at 25 °C for 24 h but not heated to reflux, the products were the diketone **17** (55%, n^{25}_D 1.4687) and the keto phosphonate **13** (32%, n^{25}_D 1.4733). Similarly, when a solution of the diketo phosphonate **12** and NaOMe in MeOH was stirred at 25 °C for 22 h but not heated to reflux, the products were the keto phosphonate **13** (43%, n^{25}_D 1.4736) and the methoxy ketone **14** (38%).

Preparation of Keto Selenide 15. After a solution of 892 mg (2.86 mmol) of PhSeSePh in 50 mL of MeOH had been treated with 324 mg (8.56 mmol) of $NaBH_4$, the resulting solution was stirred at 25 °C for 30 min. To the resulting colorless solution was added a solution of 1.00 g (4.03 mmol) of the keto phosphonate **12** in 10 mL of MeOH. Then 4.6 mL of a MeOH solution containing 20.0 mmol of NaOMe was added, and the resulting yellow solution was stirred at 25 °C for 12 h and then refluxed for 30 min. The reaction mixture (a suspension) was cooled, concentrated, and partitioned between Et_2O and H_2O. The ethereal layer was dried and concentrated to leave 850 mg of yellow liquid containing (TLC, silica gel coating with an ethyl acetate–hexane eluent, 1:9, v/v) the keto selenide **15** (R_f 0.19) and an identified impurity (R_f 0.54). Chromatography on silica gel separated 260 mg (24%) of the keto selenide **15** as a pale yellow liquid; distillation of a portion of this liquid in a short-path still (163–165 °C and 1.1 mm) separated a pure sample of the keto selenide **15** as a colorless liquid: n^{25}_D 1.5972; IR (CCl_4) 1710 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 7.1–7.7 (5 H, m, aryl CH), 1.2–2.6 (11 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 280 (M^+, 12), 278 (M^+, 6), 123 (68), 95 (100), 81 (24), 67 (41), 55 (23), 43 (96), 42 (31), 41 (56), 40 (22), 39 (26).

Anal. Calcd for $C_{14}H_{16}OSe$: C, 60.21; H, 5.79; M_r, 280.0362. Found: C, 60.10; H, 5.87; M_r, 280.0390.

Preparation of Unsaturated Acid 18b. A cold (−78 °C) mixture of 23.32 g (0.23 mol) of freshly distilled methyl methacrylate (bp 99–101 °C, n^{25}_D 1.4121), 40 mL of 1,3-butadiene, and 10 mg of 2,6-di-*tert*-butylphenol (an inhibitor) was sealed in an autoclave under an N_2 atmosphere and then heated to 125 °C for 10 h. The resulting mixture was fractionally distilled to separate 13.67 g of early fractions [bp 60–63 °C (1.2 mm), n^{25}_D 1.4592] containing (TLC, silica coating with an diethyl ether/hexane eluent, 1:1, v/v) a mixture of the desired ester **18a** (R_f 0.63) and several more rapidly eluted impurities. Subsequent distillation fractions contained 21.30 g of the ester **18a**: bp 64–65 °C (1.2 mm): n^{25}_D 1.4578 [lit.[18] bp 64–65 °C (1.0 mm), n^{20}_D 1.4600]; IR (CCl_4) 1735 (ester C=O), 1655 cm^{-1} (C=C); NMR (CCl_4) δ 5.55 (2 H, br s, vinyl CH), 3.60 (3 H, s, OCH_3), 1.2–2.8 (6 H, m, CH_2), 1.18 (3 H, s, CH_3).

A mixture of 44.23 g (0.290 mol) of the ester **18a**, 24 g (0.6 mol) of NaOH, and 200 mL of H_2O was refluxed with stirring for 5 h and then cooled and extracted with Et_2O. The resulting aqueous phase was acidified with aqueous HCl, and then extracted with Et_2O. After the acidic ethereal extract had been washed with aqueous NaCl, dried, and concentrated, the residual colorless solid was recrystallized from an acetone–hexane mixture. The unsaturated acid **18b** separated as 33.29 g (82%) of colorless prisms: mp 76–77 °C (lit.[18] mp 78–79 °C; IR (CCl_4) 2600–3200 (br, assoc OH), 1705 cm^{-1} (carboxyl C=O); NMR (CCl_4) δ 5.60 (2 H, narrow multiplet, vinyl CH), 1.4–2.8 (6 H, m, CH_2), 1.30 (3 H, s, CH_3).

Preparation of Lactones 19 and 20. To a solution prepared from 33.29 g (0.240 mol) of the acid **18b**, 100.2 g (1.20 mol) of $NaHCO_3$, 500 mL of H_2O, and 500 mL of THF were added successively 47.81 g (0.29 mol) of KI and 184.74 g (0.72 mol) of I_2. The resulting purple brown mixture was stirred at 25 °C under an N_2 atmosphere for 16 h and then partitioned between Et_2O and saturated aqueous $Na_2S_2O_3$. The ethereal layer was washed with aqueous NaCl, dried, and concentrated to leave 63 g of the crude iodo lactone **19**. Recrystallization from a diethyl ether–pentane mixture separated 59.78 g (96%) of the pure iodo lactone **19** as colorless prisms, mp 103–103.3 °C dec (lit.[19] mp 103.5–104 °C). The iodo lactone **19** was readily sublimed (80–90 °C at 0.9 mm) to give material melting at 103–103.2 °C dec; since the pure material was degraded upon exposure to light, it was stored in a dark bottle. The spectral properties follow: IR (CCl_4) 1805 (shoulder), 1790 cm^{-1} (γ-lactone C=O); NMR (CCl_4) δ 4.4–4.9 (2 H, m, CHO and CHI), 1.4–2.9 (6 H, m, CH_2), 1.12 (3 H, s, CH_3); mass spectrum, *m/e* (rel intensity) 266 (M^+, 0.4), 139 (34), 127 (19), 111 (13), 95 (100), 93 (13), 79 (17), 77 (14), 67 (23), 55 (25), 41 (14), 39 (16).

Anal. Calcd for $C_8H_{11}IO_2$: C, 36.11; H, 4.17; I, 47.70. Found: C, 36.11; H, 4.21; I, 47.70.

A solution of 58.16 g (0.22 mol) of the iodo lactone **19**, 30 mg of azoisobutyronitrile and 70.43 g (0.24 mol) of *n*-Bu_3SnH in 250 mL of benzene was refluxed under an N_2 atmosphere for 16 h and then concentrated under reduced pressure. A solution of the residual semisolid in 300 mL of Et_2O was stirred with 500 mL of aqueous 10% KF for 30 min and then filtered to remove the *n*-Bu_3SnF polymer.[20] The combined ethereal layer and the ether extract of the aqueous phase were dried and concentrated. The residual colorless semisolid was distilled to separate 24.98 g (81%) of the lactone **20** [bp 85–87 **C** (3.0 mm) [lit.[21] bp 102–104 °C (10 mm)]] that crystallized as hygroscopic colorless prisms: mp 35.5–36 °C; IR (CCl_4) 1790 cm^{-1} (γ-lactone C=O); NMR ($CDCl_3$) δ 4.5–4.9 (1 H, m, CHO), 0.9–2.5 (11 H, m, aliphatic CH including a CH_3 singlet at 1.20); mass spectrum, *m/e* (rel intensity) 140 (M^+, 0.7), 98 (16), 97 (21), 96 (34), 81 (100), 68 (32), 67 (28), 55 (22), 41 (20), 39 (21).

Preparation of Diketo Sulfone 21. To a cold (0 °C) solution containing 0.11 mol of *n*-BuLi in 74.5 mL of hexane was added, dropwise and with stirring during 1 h, a solution of 10.94 g (0.12 mol) of $CH_3SO_2CH_3$ in 150 mL of DME. The cooling bath was removed, and a solution of 6.52 g (47 mmol) of the lactone **20** in 40 mL of DME was added dropwise and with stirring during 15 min. The resulting mixture (a white suspension) was refluxed for 12 h at which time TLC analysis (silica gel with a $CHCl_3$–Et_2O eluent) indicated that all of the starting lactone **20** (R_f 0.61) was gone. The solution was acidified with excess aqueous 1 M HCl and extracted with $CHCl_3$. After the organic extract had been washed with aqueous NaCl, it was dried and concentrated to leave the crude hydroxy sulfone as 9.90 g of yellow liquid. Since a variety of attempts to obtain a pure sample of this hydroxy keto sulfone were unsuccessful, the crude product was oxidized to the diketone **21**. The spectral properties of the crude hydroxy keto

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(19) Stork, G.; Logusch, E. W. *Tetrahedron Lett.* **1979**, 3361.
(20) Isolation procedure: Lieber, J. E.; Jacobus, J. *J. Org. Chem.* **1979**, *44*, 449.
(21) Ismailov, A. G.; Rustov, M. A.; Akhmedov, A. A. *J. Org. Chem. USSR (Engl. Transl.)* **1977**, *13*, 1310.

sulfone are as follows: IR ($CHCl_3$) 3580, 3490 (OH), 1710 cm^{-1} (C=O); NMR ($CDCl_3$) δ 3.4–4.7 (4 H, m, OH, CHO, and a CH_2 singlet at 4.40), 3.17 (3 H, s, SO_2CH_3), 1.2–2.4 (8 H, m, aliphatic CH), 1.20 (3 H, s, CH_3); mass spectrum, *m/e* (rel intensity) 138 (13), 97 (22), 96 (41), 95 (100), 94 (23), 81 (89), 79 (43), 69 (26), 68 (31), 67 (41), 55 (44), 43 (29), 41 (56), 39 (30).

A cold (0–5 °C) solution of 2.00 g (8.5 mmol) of the hydroxy sulfone in 100 mL of acetone was treated with 2.13 mL (1.0 equiv) of aqueous 8 N H_2CrO_4 (Jones reagent). The resulting mixture was stirred for 5 min and then partitioned between H_2O and $CHCl_3$. The organic layer was washed with aqueous NaCl, dried, and concentrated to leave 1.54 g of the crude diketo sulfone **21** as a yellow liquid. This material was chromatographed on silica gel with an Et_2O eluent to separate early fractions containing the aldol product **22** as a colorless solid, mp 140–170 °C, and later fractions containing the diketo sulfone **21** as a colorless solid, (mp 51–52 °C).

The more rapidly eluted product was recrystallized from a chloroform–hexane mixture to separate 462 mg of the aldol product **22** (a mixture of epimers) as colorless prisms melting in the range 140–170 °C. The melting point of this mixture of ketol epimers **22** was not sharpened by further recrystallization. The spectral properties of the ketol **22** follow: IR ($CHCl_3$) 3555 (OH), 1745 cm^{-1} (cyclopentanone C=O); NMR ($CDCl_3$) δ 3.83 (1 H, s, $COCHSO_2$), 3.50 (1 H, br, OH), 3.12 (3 H, 2 partially resolved singlets SO_2CH_3), 1.3–2.8 (8 H, m, aliphatic CH), 1.17 (3 H, 2 partially resolved singlets, CH_3); mass spectrum, *m/e* (rel intensity) 232 (M^+, 7), 189 (44), 153 (23), 112 (23), 111 (100), 97 (70), 79 (32), 69 (45), 55 (46), 43 (29), 41 (29).

Anal. Calcd for $C_{10}H_{16}O_4S$: C, 51.70; H, 6.96; S, 13.80. Found: C, 51.70; H, 6.94; S, 13.82.

The later fractions were recrystallized from a chloroform–hexane mixture to separate 1.04 g (69%) of the diketo sulfone **21** as colorless prisms: mp 64–65 °C; IR ($CHCl_3$) 1742, 1712 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 4.20 (2 H, br s, $COCH_2SO_1$), 3.1 (3 H, s, SO_2CH_3), 1.5–2.9 (8 H, m, aliphatic CH), 1.26 (3 H, s, CCH_3); mass spectrum, *m/e* (rel intensity) 232 (M^+, 2.5), 189 (21), 111 (100), 97 (36), 69 (24), 55 (76), 43 (20), 41 (30).

Anal. Calcd for $C_{10}H_{16}O_4S$: C, 51.70; H, 6.96; S, 13.80. Found: C, 51.77; H, 6.96; S, 13.76.

Preparation of Ketol 22. A. With *t*-BuMgCl. To a cold (0 °C solution of 154 mg (0.66 mmol) of the diketo sulfone **21** in 10 mL of DME was added, dropwise and with stirring during 1 min, 0.95 mL of a THF solution containing[22] 0.67 mmol of *t*-BuMgCl. The resulting colorless solution turned a light yellow-green color as the solution warmed to 25 °C, and a white precipitate separated after 30 min. The resulting white suspension was heated to reflux (with initial solution of the precipitate and subsequent separation of a yellow oil) for 2 h and then cooled to 25 °C and stirred for 24 h. The resulting suspension was partitioned between aqueous 1 M HOAc and $CHCl_3$. The $CHCl_3$ layer was dried and concentrated, and the residual oil was partitioned between EtOAc and aqueous 0.5 M HCl. The EtOAc layer was dried and concentrated to leave 155 mg of the crude aldol product **22**. Recrystallization from a chloroform–hexane mixture separated 150 mg (98%) of the ketol **22** (a mixture of epimers) as colorless prisms, mp 140–170 °C, that were identified with previously described material by comparison of IR and NMR spectra.

B. With NaOH. A solution of 70 mg (0.30 mmol) of the diketo sulfone **21** in 10 mL of THF was mixed with a solution of 80 mg (2.0 mmol) of NaOH in 15 mL of H_2O, and the resulting mixture was stirred at 25 °C for 39 h. The resulting mixture was partitioned between aqueous 1 M HCl and $CHCl_3$, and the $CHCl_3$ layer was washed with aqueous NaCl, dried, and concentrated. The residual colorless solid (67 mg) was recrystallized from a chloroform–hexane mixture to separate 58 mg (83%) of the ketol **22** (a mixture of epimers) as colorless needles, mp 140–160 °C. The material was identified with the previously described sample by comparison of NMR spectra.

Preparation of Ketol 23a and Its Esters 23b, 26a, and 26b. A suspension of 4.18 g (24 mmol) of K_2HPO_4 and 1.36 g (5.9 mmol) of the sulfone **22** in 100 mL of cold (0 °C) MeOH was treated with 6.90 g of a 6% Na in mercury amalgam,[23,24] and the resulting mixture was stirred at 25 °C for 3 h. After the mixture had been filtered and the residue washed with 15 mL of MeOH, the combined filtrates were partitioned between aqueous NaCl and $CHCl_3$. The $CHCl_3$ solution was dried and concentrated to leave 684 mg (76%) of the crude ketol **23a** as a colorless liquid. Distillation in a short-path still separated the ketol **23a** as a colorless liquid, bp 79–80 °C (0.5 mm); that solidified on standing, mp 25–26 °C. The spectral properties of the ketol **23a** follow: IR (CCl_4) 3610, 3460 (OH), 1745 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 3.43 (1 H, br s, OH), 2.26 (2 H, s, CH_2CO), 0.8–2.2 (11 H, m, aliphatic CH including a CH_3 singlet at 1.05); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 218.3 (s), 73.4 (s), 52.5 (s), 50.8 (t, 2 C atoms), 37.8 (t), 36.7 (t), 20.6 (t), 19.7 ppm (q); mass spectrum, *m/e* (rel intensity) 154 (M^+, 7), 111 (67), 97 (100), 95 (29), 94 (36), 69 (30), 55 (37), 43 (56), 41 (44), 39 (37).

Anal. Calcd for $C_9H_{14}O_2$: M_r, 154.0990. Found: M_r, 154.0954.

Since attempts to obtain an analytically pure sample of the ketol **23a** were complicated by the rapidity with which the material reacted with moist air (apparently to form a hydrate), the ketol **23a** was further characterized as its acetate **23b**. A solution of 486 mg (3.2 mmol) of the ketol **23a** in 10 mL of Ac_2O was refluxed for 1.5 h and then cooled and stirred with aqueous $NaHCO_3$ to hydrolyze the unchanged Ac_2O. After the resulting mixture had been extracted with $CHCl_3$, the $CHCl_3$ extract was washed with aqueous NaCl, dried, and concentrated. The residual yellow liquid was chromatographed on silica gel to separate 74 mg of uncharacterized early fractions (eluted with CCl_4) and 482 mg of the acetate **23b** (eluted with Et_2O). Distillation in a short-path still (115–120 °C at 3.0–3.5 mm) separated 465 mg (74%) of the acetoxy ketone **23b** as a colorless liquid: n^{25}_D 1.4704; IR (CCl_4) 1740 cm^{-1} (br, ester and cyclopentanone C=O); ^1H NMR (CCl_4) δ 0.9–2.7 (m, aliphatic CH including CH_3 singlets at 1.98 and 1.00); mass spectrum, *m/e* (rel intensity) 196 (M^+, 0.8), 121 (17), 108 (51), 93 (39), 43 (100), 41 (19).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22; M_r, 196.1095. Found: C, 67.34; H, 8.26; M_r, 196.1075.

To a cold (0 °C) solution of 553 mg (3.9 mmol) of the ketol **23a** in 15 mL of pyridine was added, dropwise and with stirring, 4.50 g (39 mmol) of freshly distilled $MeSO_2Cl$. The resulting solution, from which a solid slowly separated, was stirred at 0–5 °C for 18 h and then partitioned between $CHCl_3$ and aqueous 1 M HCl. After the $CHCl_3$ layer had been washed successively with aqueous HCl, with aqueous $NaHCO_3$, and with H_2O, the solution was dried and concentrated. The residual orange liquid (1.00 g) was distilled to separate 710 mg (85%) of the sulfonate ester **26a** as a pale yellow liquid: bp 116–118 °C (0.05 mm); n^{25}_D 1.4913; IR ($CHCl_3$) 1750 (cyclopentanone C=O), 1340, 1168 cm^{-1} (OSO_2R); ^1H NMR ($CDCl_3$) δ 3.10 (3 H, s, OSO_2CH_3), 2.80 (2 H, br, $COCH_2$), 1.0–2.65 (11 H, m, aliphatic CH including a CH_3 singlet at 1.13); mass spectrum, *m/e* (rel intensity) 232 (M^+, 1), 121 (15), 111 (19), 109 (39), 108 (100), 107 (20), 95 (21), 94 (25), 93 (75), 79 (37), 67 (31), 55 (36), 41 (35), 39 (25).

Anal. Calcd for $C_{10}H_{16}O_4S$: C, 51.70; H, 6.96; S, 13.80. Found: C, 51.91; H, 6.99; S, 13.69.

A cold (0–5 °C) mixture of 1.29 g (8.4 mmol) of the ketol **23a**, 3.21 g (16.9 mmol) of *p*-$CH_3C_6H_4SO_2Cl$, and 25 mL of pyridine was stirred for 15 min, the the resulting solution was allowed to warm to 25 °C, and stirring was continued for 36 h. The final reddish-pink solution was poured into 200 mL of cold H_2O, and the crude solid tosylate **26b** that separated was collected on a filter and washed with H_2O. The aqueous filtrates were extracted with $CHCl_3$, and the organic extract was washed successively with aqueous 1 M HCl and with aqueous NaCl. The $CHCl_3$ extract was then dried and concentrated to recover 170 mg (13%) of the starting ketol **23a**. The crude tosylate was recrystallized from a carbon tetrachloride–hexane mixture to separate 2.12 g (82%) of the tosylate **26b** as colorless prisms: mp 97–98 °C; IR (CCl_4) 1753 cm^{-1} (cyclopentanone C=O); ^1H NMR ($CDCl_3$) δ 7.2–8.0 (4 H, m, aryl CH), 2.68 (2 H, br s, $COCH_2$), 2.46 (3 H, s, aryl CH_3), 1.0–2.4 (11 H, m, aliphatic CH including a CH_3 singlet at 1.02);

(22) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(23) Reduction procedure: Trost, B. M.; Weber, L.; Strege, P.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3426.

(24) The amalgam as prepared by the procedure of Brasen and Hauser Brasen, W. R.; Hauser, C. R. "Organic Syntheses"; Wiley: New York, 1963; Collect. Vol. 4, 508.

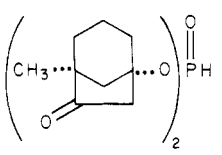
mass spectrum, m/e (rel intensity) 308 (M^+, <1), 155 (15), 153 (19), 109 (31), 108 (100), 93 (53), 91 (51), 79 (15), 67 (19), 65 (16), 55 (32), 41 (23).

Anal. Calcd for $C_{16}H_{20}O_4S$: C, 62.30; H, 6.55; S, 10.40. Found: C, 62.32; H, 6.57; S, 10.37.

In an attempt to convert the ketol **23a** to the corresponding bromo ketone,[4] a cold (5 °C) solution of 2.43 g (15.8 mmol) of the ketol **23a** in 20 mL of PhH was treated with a solution of 1.71 g (6.3 mmol) of PBr_3 in 10 mL of PhH. The resulting solution was stirred at 25 °C for 12 h and then partitioned between $CHCl_3$ and H_2O. After the organic layer had been washed with aqueous NaCl, dried, and concentrated, the residual liquid was chromatographed on silica gel with an Et_2O eluent. The intermediate liquid fractions (2.52 g) were combined and distilled in a short-path still (87–90 °C and 0.01 mm) to separate 2.51 g (90%) of the phosphite ester **49** as a colorless liquid: n^{25}_D 1.5060; IR (CCl_4) 2430 (PH), 1752 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 2.61 (4 H, br, $COCH_2$), 0.9–2.5 (22 H, m, aliphatic CH including a CH_3 singlet at 1.04); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 215.0 (s, 2 C atoms), 83.5 (s, 2 C atoms), 51.8 (s, 2 C atoms), 49.6 (t, 2 C atoms), 36.2 (t, 6 C atoms), 20.3 (t, 2 C atoms), 19.5 ppm (q, 2 C atoms); mass spectrum, m/e (rel intensity) 354 (M^+, 1.6), 136 (72), 121 (75), 109 (100), 108 (89), 93 (32), 67 (23), 41 (28).

Anal. Calcd for $C_{18}H_{27}O_5P$: C, 61.00; H, 7.69. Found: C, 60.62; H, 7.68.

When a solution of 710 mg (2.0 mmol) of the phosphite **49** and



49

9 mL (57 mmol) of Et_3N in 10 mL of MeOH was refluxed for 5 h, the resulting neutral organic product was 521 mg (77%) of the methoxy ketone **25**: n^{25}_D 1.4723. This product was identified with an authentic sample by comparison of IR and ^1H NMR spectral data.

Reaction of Sulfonate Ester 26a with Et_3N. A. With Added MeOH. When a solution of the sulfonate **26a** in MeOH was refluxed for 12 h or when a solution of the sulfonate **26a** in a MeOH–Et_3N mixture was stirred at 25 °C for 12 h, only the unchanged starting material **26a** was recovered. A solution of 625 mg (2.7 mmol) of the sulfonate **26a** and 1.0 mL (7.2 mmol) of Et_3N in 5 mL of MeOH was refluxed for 14 h. The resulting orange-brown suspension was concentrated and then partitioned between aqueous 1 M HCl and $CHCl_3$. The $CHCl_3$ layer was washed with aqueous NaCl and with aqueous $NaHCO_3$ and then dried and concentrated. The residual orange liquid (459 mg) was triturated with a chloroform–hexane mixture (1:9, v/v) to separate 37 mg (4%) of the crude disulfonate ester **28** as colorless prisms, mp 126–130 °C. A portion of the remaining crude methoxy ketone **25**, 415 mg (92%) of a yellow-orange liquid, was distilled in a short-path still (89–91 °C at 0.05 mm) to separate the pure methoxy ketone **25** as a colorless liquid; n^{25}_D 1.4722; IR (CCl_4) 1745 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 3.20 (3 H, s, OCH_3), 2.21 (2 H, br, $COCH_2$), 0.8–2.1 (11 H, m, aliphatic CH including a CH_3 singlet at 1.08); mass spectrum, m/e (rel intensity) 168 (M^+, 54), 153 (24), 115 (100), 111 (63), 72 (23), 55 (21), 41 (45), 39 (46); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 217.5 (s), 78.1 (s), 51.8 (s), 50.4 (q), 47.8 (t), 47.6 (t), 36.9 (t), 32.6 (t), 20.3 (t), 19.8 ppm (q).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59; M_r, 168.1146. Found: C, 71.29; H, 9.60; M_r, 168.1151 (mass spectrum).

The crude disulfonate ester **28** was recrystallized from a $CHCl_3$–CCl_4 mixture to separate the pure diester **28** as colorless prisms, mp 133–134 °C. This material was identified with a subsequently described sample by comparison of IR, NMR, and mass spectral data.

B. With Added Furan. A solution of 184 mg (0.80 mmol) of the sulfonate ester **26a** in 10 mL of furan and 10 mL of THF was treated with 6.0 mL (43 mmol) of Et_3N. The resulting mixture, which turned red-orange in color with the separation of a precipitate, was refluxed (50 °C) with stirring for 19.5 h during which time the color lightened and the precipitate redissolved. After the mixture had been partitioned between H_2O and $CHCl_3$, the organic layer was dried and concentrated. Chromatography of the residual brown liquid on silica gel with a $CHCl_3$ eluent separated 148 mg of yellow liquid, which partially crystallized on standing. Washing with CCl_4 left 55 mg (22%) of the insoluble crude disulfonate **28**. This material was recrystallized from a $CHCl_3$–CCl_4 mixture to separate the disulfonate **28** as colorless prisms; mp 133–134 °C; IR ($CHCl_3$) 1340, 1173 cm^{-1} (OSO_2); ^1H NMR ($CDCl_3$) δ 4.6–5.0 (1 H, m, vinyl CH), 3.00 (6 H, s, CH_3SO_3), 1.0–2.9 (11 H, m, aliphatic CH including a CH_3 singlet at 1.15); mass spectrum, m/e (rel intensity) 269 (2), 137 (100), 121 (57), 120 (30), 111 (20), 109 (33), 105 (24), 95 (41), 93 (98), 92 (25), 79 (38), 67 (37), 55 (34), 43 (24), 41 (30).

Anal. Calcd for $C_{11}H_{18}O_6S_2$: C, 42.56; H, 5.86; S, 20.66. Found: C, 42.55; H, 5.88; S, 20.66.

The mother liquors remaining after separation of the disulfonate **28** were concentrated, and the residual crude furan adduct **31**, 93 mg (58%) of yellow-orange liquid, was distilled in a short-path still (70–75 °C at 1.0–1.3 mm). The furan adduct **31** (mixture of stereoisomers) was collected as 52 mg of colorless liquid: IR (CCl_4) 1740 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 6.2–6.66 (2 H, m, vinyl CH), 4.90 (1 H, br, allylic CHO), 4.45 (1 H, br, allylic CHO), 2.6–3.0 (1 H, m, COCH), 0.7–2.5 (11 H, m, aliphatic CH including CH_3 singlets at 0.98 and 0.83); mass spectrum, m/e (rel intensity) 204 (M^+, 6), 176 (24), 121 (100), 108 (40), 93 (31), 91 (34), 80 (23), 79 (26), 77 (27), 55 (26), 41 (34), 39 (43).

One method for obtaining the major stereoisomer **31a** of adduct **31** involved formation of its (2,4-dinitrophenyl)hydrazone. To a warm solution of 129 mg (0.65 mmol) of (2,4-dinitrophenyl)-hydrazine, 0.3 mL of aqueous 12 M HCl, and 10 mL of MeOH was added, dropwise and with stirring during 1 min, a solution of 133 mg (0.65 mmol) of the adduct **31** in 1 mL of MeOH. The resulting solution was warmed to ca. 45–50 °C for 1 min and then cooled and concentrated under reduced pressure. The residual yellow-orange solid was recrystallized successively from aqueous MeOH and then from a $CHCl_3$–CCl_4 mixture to separate 240 mg (96%) of the 2,4-DNP of adduct **31a** as an orange solid, mp 190–191 °C dec. Two additional recrystallizations from MeOH afforded the 2,4-DNP of adduct **31a** as orange prisms: 198–199 °C dec; IR ($CHCl_3$) 3420, 3320 (NH), 1619 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 11.2 (1 H, s, NH), 7.8–8.5 (3 H, m, aryl CH), 6.4–6.8 (2 H, m, vinyl CH), 5.40 (1 H, br s, CHO), 4.63 (1 H, br s, CHO), 2.35 (1 H, br, N=CCH), 1.0–2.3 (11 H, m, aliphatic CH including a CH_3 singlet at 1.30); mass spectrum, m/e (rel intensity) 384 (M^+, 2), 316 (66), 281 (33), 108 (100), 106 (23), 105 (22), 93 (40), 91 (67), 79 (39), 77 (30), 55 (20), 41 (29), 39 (23).

Anal. Calcd for $C_{19}H_{20}N_4O_5$: C, 59.37; H, 5.24; N, 14.58. Found: C, 59.31; H, 5.26; N, 14.57.

Reaction of Sulfonate Ester 26b with Et_3N and Furan. A solution of 1.18 g (3.8 mmol) of the tosylate **26b** and 0.64 mL (4.6 mmol) of Et_3N in 25 mL of furan and 25 mL of DME was refluxed for 48 h during which time a precipitate formed and slowly redissolved. The reaction mixture was concentrated, triturated with CCl_4, and filtered to remove the triethylammonium salt. The filtrate was concentrated and chromatographed on silica gel with an Et_2O eluent. The early fractions (615 mg) were distilled in a short-path still (110–115 °C and 0.1 mm) to separate 586 mg (76%) of the mixture of stereoisomeric furan adducts **31** as a colorless liquid that solidified as colorless needles, mp 68–74 °C. The ^1H NMR and ^{13}C NMR of this mixture **31** suggested that it contained about 80% of the major stereosiomer **31a**. The ^{13}C NMR spectrum ($CDCl_3$) of the mixture of stereoisomers **31** contained the following peaks attributable to the major stereoisomer (**31a**: ($CDCl_3$, multiplicity in off-resonance decoupling) 214.2 (s), 137.1 (d), 132.8 (d), 82.6 (d), 78.6 (d), 57.0 (d), 54.2 (s), 49.6 (s), 45.2 (t), 36.3 (t), 31.1 (t), 22.2 (t), 20.1 ppm (q). In addition the following ^{13}C NMR peaks attributable to the minor stereoisomer were present: 212.8, 138.8, 131.8, 83.2, 77.1, 56.6, 55.3, 49.8, 45.6, 36.1, 33.3, 21.0, and 20.4 ppm.

The mixture **31** was chromatographed on silica gel impregnated with $AgNO_3$ by employing Et_2O as the eluent to separate later fractions containing (^1H NMR analysis) the major stereoisomer **31a**. This material was rechromatographed on silica gel and then distilled in a short-path still (100–103 °C and 0.4 mm) to separate

the adduct **31a** as a colorless liquid that solidified as colorless prisms: mp 70–71 °C; IR (CCl_4) 1740 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 6.2–6.6 (2 H, m, vinyl CH), 4.90 (1 H, partially resolved multiplet, CHO), 4.45 (1 H, partially resolved multiplet, CHO), 0.9–2.2 (11 H, m, aliphatic CH including a CH_3 singlet at 0.98); mass spectrum, *m/e* (rel intensity) 204 (M^+, 5), 176 (24), 121 (100), 108 (39), 93 (28), 91 (41), 80 (20), 79 (27), 77 (24), 41 (22), 39 (30).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.35; H, 7.91.

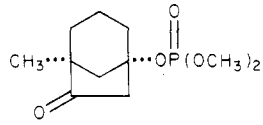
A portion of this adduct **31a** was recrystallized from a carbon tetrachloride–butadiene mixture to form a crystal suitable for X-ray crystallography.

Preparation of Diketo Phosphonate 24. A solution of 3.62 g (29 mmol) of $CH_3P(O)(OMe)_2$ in 20 mL of DME was added, dropwise and with stirring during 5 min, to a cold (–78 °C) solution of 29 mmol of *n*-BuLi in 20.2 mL of hexane. After the resulting cold (–78 °C) suspension had been stirred for 10 min, a solution of 1.64 g (12 mmol) of the lactone **20** in 50 mL of DME was added, dropwise and with stirring during 5 min. The resulting mixture was allowed to warm to 15 °C during 3 h and then poured into aqueous 1 M HCl and extracted repeatedly with $CHCl_3$. After the organic extract had been washed with H_2O and with aqueous NaCl, it was dried and concentrated. The crude residual hydroxy keto phosphonate amounted to 3.47 g of pale yellow liquid: IR (CCl_4) 3410 (br, OH), 1710 cm^{-1} (C=O). Since efforts to purify this crude product resulted in change or decomposition, the crude alcohol was oxidized without purification.

A cold (0–5 °C) solution of 1.00 g (3.8 mmol) of the hydroxy phosphonate in 100 mL of acetone was treated with 0.95 mL (1.0 equiv) of aqueous 8 N H_2CrO_4 (Jones reagent). After the mixture had been stirred for 10 min, it was partitioned between H_2O and $CHCl_3$. The organic layer was washed with aqueous NaCl and then dried and concentrated to leave 0.98 g of the crude diketo phosphonate as a colorless liquid. This material was distilled in a short-path still (120–135 °C at 1.1–2.6 mm) to separate 0.88 g (88%) of the diketo phosphonate **24** as a colorless liquid: IR (CCl_4) 1711 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 3.4–3.9 (6 H, m, OCH_3), 0.8–3.3 (13 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 262 (M^+, 0.3), 151 (100), 124 (87), 109 (30), 94 (25), 55 (19).

Anal. Calcd for $C_{11}H_{19}O_5P$: C, 50.37; H, 7.32. Found: C, 50.38; H, 7.31.

In another larger scale experiment distillation of the diketo phosphonate **24** (65–170 °C at 0.05–0.06 mm) resulted in substantial thermal decomposition. The major fractions (35 g) were chromatographed on silica gel with an Et_2O eluent to separate early fractions that were distilled (87–90 °C at 0.05 mm) to give 3.97 g of the keto phosphate **50** as a colorless liquid: n^{25}_D 1.4742;



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IR (CCl_4) 1750 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 3.65 (6 H, d, *J* = 11 Hz, $POCH_3$), 2.55 (2 H, br, CH_2CO), 1.0–2.4 (11 H, m, aliphatic CH including a CH_3 singlet at 1.02); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 215.4 (s), 82.8 and 82.4 (s, J_{PC} = 7.6 Hz), 54.0 and 53.8 (s, 2 C atoms, J_{PC} = 6.1 Hz), 51.9 (s), 49.2 (t, 2 C atoms), 36.2 (t), 35.6 (t), 20.3 (t), 19.5 ppm (q); mass spectrum, *m/e* (rel intensity) 262 (M^+, <1), 136 (42), 127 (100), 121 (81), 109 (31), 108 (55), 93 (34), 79 (21).

Anal. Calcd for $C_{11}H_{19}O_5P$: C, 50.37; H, 7.32. Found: C, 50.37; H, 7.30.

Later fractions from the chromatography contained 2.45 g of the subsequently described ketol **27** and subsequent fractions, eluted with EtOAc, contained 9.8 g of the diketo phosphonate **24**. These products **24** and **27** were identified with authentic samples by comparison of IR and NMR spectral data.

Reaction of Diketo Phosphonate 24 with Base. A. In MeOH. A solution of 298 mg (1.1 mmol) of the diketo phosphonate **24** in 10 mL of MeOH was mixed with a solution of 2.4 mmol of NaOMe in 1 mL of MeOH. The resulting mixture was stirred at 25 °C for 24 h and then partitioned between H_2O and $CHCl_3$. The organic layer was washed with aqueous NaCl, dried, and concentrated. The residual colorless liquid (185 mg) was distilled in a short-path still (130–132 °C at 1.0 mm) to separate 172 mg (93%) of the methoxy ketone **25** as a colorless liquid; n^{25}_D 1.4723. This product was identified with the previously described sample by comparison of IR, NMR, and mass spectral data.

B. In H_2O–THF. A solution of 2.52 g (9.6 mmol) of the diketo phosphonate **24** in 30 mL of H_2O and 30 mL of THF was treated with 5.8 mL of an aqueous solution containing 14.4 mmol of NaOH. After the resulting mixture had been stirred at 25 °C for 3 h, it was partitioned between $CHCl_3$ and aqueous 1 M HCl. The organic layer was washed successively with H_2O and with aqueous NaCl and then dried and concentrated. Distillation of the residual colorless liquid in a short-path still (84–86 °C at 0.8–1.0 mm) separated 1.29 g (87%) of the ketol **23a** as a colorless liquid that solidified on standing, mp 25–26 °C. This material was identified with a previously described sample of the ketol **23a** by comparison of IR, ^1H NMR, and mass spectral data.

In another similar experiment employing 18.5 mmol of the diketo phosphonate **24** and 18.5 mmol of NaOH, the crude liquid product was chromatographed on silica gel with an Et_2O eluent to separate early fractions containing 1.92 g (67%) of the ketol **23a** and later fractions containing 1.48 g (30%) of the subsequently described ketol **27**. Both products were identified with authentic samples by comparison of IR and ^1H NMR spectral data.

C. NaH in DME. The NaH (ca. 280 mg or 12 mmol) obtained by washing 470 mg of a 60% dispersion of NaH in oil with hexane was suspended in 30 mL of DME, and then 1.60 g (6.1 mmol) of the diketo phosphonate **24** was added, dropwise and with stirring during 2 min. After the mixture had been stirred for 1 h, the tan slurry containing a thick precipitate was partitioned between $CHCl_3$ and aqueous 1 M HCl. The organic layer was washed with aqueous NaCl, dried, and concentrated. Chromotography of the residual amber liquid on silica gel with an Et_2O eluent separated 1.29 g (80%) of the crude ketol **27** as a pale yellow liquid. Distillation in a short-path still (120–126 °C and 0.03–0.05 mm) afforded the pure ketol **27** (a mixture of diastereoisomers) as a colorless liquid: n^{25}_D 1.4976; IR (CCl_4) 3400 (OH), 1745 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 4.30 (1 H, br, OH), 3.6–4.0 (6 H, m, OCH_3), 3.2–3.4 (1 H, m, CHCO of epimers), 1.0–2.3 (11 H, m, aliphatic CH including a CH_3 singlet at 1.02); mass spectrum, *m/e* (rel intensity) 262 (M^+, 1), 220 (26), 219 (20), 151 (100), 109 (21).

Anal. Calcd for $C_{11}H_{19}O_5P$: C, 50.37; H, 7.32; M_r, 262.0965. Found: C, 50.39; H, 7.32; M_r, 262.1099 (mass spectrum).

Samples of the ketol **27** were recovered unchanged after being heated in refluxing CCl_4 or being stirred with Et_3N at 25 °C for 10 h at 25 °C. A solution of 2.13 g (8.1 mmol) of the ketol **27** and 8.5 mmol of NaOH in 33 mL of H_2O and 30 mL of THF was stirred at 25 °C for 2 h and then partitioned between $CHCl_3$ and aqueous 1 M HCl. The organic product, isolated in the usual way, was distilled to separate 1.20 g (96%) of the ketol **23a** that was identified by comparison of IR and NMR spectral data.

Pyrolysis of Furan Adduct 31. A solution of 322 mg (1.58 mmol) of the adduct **31** in 4.0 mL of cyclohexane was heated to 240 °C in a sealed tube for 3 h and then cooled and concentrated. The residual yellow semisolid (308 mg) contained (TLC and ^1H NMR analyses) a mixture of the starting adduct **31**, the product **32**, and several minor unidentified components. The material was triturated with CCl_4 to leave the crude adduct **32**, mp 220–224 °C. Recrystallization from chloroform–hexane separated 110 mg (41%) of the adduct **32** as colorless prisms, mp 242–243 °C; IR (CCl_4) 1730 cm^{-1} (cyclopentanone C=O); ^1H NMR ($CDCl_3$, 300 MHz) δ 4.64 (1 H, s, CHO), 4.07 (1 H, s, CHO), 3.02 (1 H, 3-line multiplet, CH), 2.61 (1 H, m, CH), 2.34 (1 H, br s, CH), 0.9–2.2 (23 H, m, aliphatic CH including CH_3 singlets at 1.01 and 0.99); mass spectrum, *m/e* (rel intensity) 340 (M^+, 9), 272 (32), 188 (33), 135 (41), 121 (47), 108 (35), 105 (36), 95 (73), 93 (41), 91 (63), 81 (30), 79 (47), 77 (35), 67 (34), 55 (57), 41 (100), 39 (43).

Anal. Calcd for $C_{22}H_{28}O_3$: M_r, 340.2031. Found: M_r, 340.2022 (mass spectrum).

Preparation of Diketo Phosphonate 34. A cold solution of the lithium salt **11** was prepared by adding a solution of 728 mg (5.9 mmol) of $CH_3P(O)(OMe)_2$ in 20 mL of THF, dropwise and with stirring during 5 min, to a cold (–65 °C) solution of 5.4 mmol of *n*-BuLi in 3.7 mL of hexane. After this cold (–65 °C) solution had been stirred for 15 min, a solution of 346 mg (2.1 mmol) of

the previously described[25] lactone **33a** in 7 mL of THF was added, dropwise and with stirring during 10 min. The resulting mixture was allowed to warm to 0 °C during 3 h and then poured with aqueous 1 M HCl and extracted repeatedly with $CHCl_3$. The $CHCl_3$ extract was washed with H_2O and with aqueous NaCl and then dried and concentrated. The residual crude hydroxy keto phosphonate **33**, 600 mg of yellow liquid, was used in the next step without further purification: IR (CCl_4) 3420 (OH), 1710 cm^{-1} (C=O).

A cold (0–5 °C) solution of 600 mg (2.1 mmol) of the hydroxy keto phosphonate **33** in 75 mL of acetone was treated with 0.53 mL (1.0 equiv) of aqueous 8 N H_2CrO_4 (Jones reagent) and then stirred for 10 min. After the mixture had been partitioned between H_2O and $CHCl_3$, the organic layer was washed with aqueous NaCl, dried, and concentrated. The residual yellow-green liquid (565 mg) was chromatographed on silica gel. After separation of initial fractions (23 mg of yellow semisolid) eluted with Et_2O, continued elution with EtOAc separated 535 mg (88%) of the diketo phosphonate **34** as a pale yellow oil. Distillation in a short-path still (90–94 °C at 1.0–1.5 mm) afforded the diketone **34** as a pale yellow liquid: n^{25}_D 1.4890; IR (CCl_4), 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 3.5–4.0 (6 H, m, OCH_3), 1.0–3.4 (15 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 288 (M^+, 0.3), 151 (45), 137 (29), 124 (100), 109 (22), 94 (42), 79 (17).

Anal. Calcd for $C_{13}H_{21}O_5P$: M_r, 288.1121. Found: M_r, 288.1105.

Preparation of Methoxy Ketone 36. A solution of 194 mg (0.67 mmol) of the diketo phosphonate **34** in 7 mL of MeOH was mixed with 151 mg (1.42 mmol) of anhydrous Na_2CO_3, and the resulting suspension was refluxed with stirring for 9 h. The resulting reaction mixture was concentrated under reduced pressure, and the semisolid residue was extracted with CCl_4. Concentration of the CCl_4 extract left 143 mg of the crude methoxy ketone as a yellow liquid. Distillation in a short-path still (82–94 °C at 1.5–2.0 mm) afforded 108 mg (83%) of the methoxy ketone **36** as a colorless liquid: n^{25}_D 1.4981; IR (CCl_4) 1746 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 3.20 (3 H, s, OCH_3), 2.30 (2 H, s, CH_2CO), 1.0–2.2 (13 H, m, aliphatic CH); ^{13}C NMR ($CDCl_3$, multiplicity in off-resonance decoupling) 215.9 (s), 78.0 (s), 61.8 (s), 50.5 (q), 48.0 (t), 44.3 (d), 39.7 (t), 31.2 (t), 30.4 (t), 29.7 (t), 23.1 (t, two C atoms); mass spectrum, *m/e* (rel intensity) 194 (M^+, 63), 152 (23), 151 (69), 125 (23), 124 (100), 123 (27), 120 (46), 91 (39), 79 (39), 67 (22), 43 (24), 41 (36), 39 (26).

Anal. Calcd for $C_{12}H_{18}O_2$: M_r, 194.1302. Found: M_r, 194.1334.

Preparation of Unsaturated Ester 40. Previously described procedures[12] were used to prepare the bromo ketal **37**, and the following modified procedure was utilized to prepare the acid **39**. To a cold (−50 °C) solution of 3.01 g (10.6 mmol) of the bromo ketal **37** in 150 mL of Me_2O (bp −24 °C) was added, dropwise and with stirring during 5 min, 7.1 mL of a hexane solution containing 10.6 mmol of *n*-BuLi. After the resulting solution had been stirred for 10 min, a stream of CO_2 gas was passed through the solution for 20 min. The resulting mixture was then allowed to warm to −20 °C and partitioned between Et_2O and H_2O. The ether layer containing neutral products was separated, and the aqueous phase was acidified to pH 4 with aqueous HCl and then extracted with Et_2O. After this ethereal extract had been washed with aqueous NaCl, dried, and concentrated, the residual solid acid **39** (2.11 g, mp 187–189 °C dec) was recrystallized from a $CHCl_3$–Et_2O mixture to separate 2.10 g (70%) of the acid **39** as cream-colored needles, mp 195–197 °C dec (lit.[12] mp 195–198 °C dec). The acid **39** was identified with previously described[12] material by comparison of IR and NMR spectral data. Concentration of the initial Et_2O solution containing neutral products afforded 0.56 g (26%) of the crude, known[12] olefinic ketal **38** as a brown liquid.

Reaction of the ketal acid **39** with CH_2N_2 formed the ketal ester **40**, mp 113–115 °C (lit.[12] mp 114.8–115.3 °C), that was identified with previously described[12] material by comparison of IR and NMR spectral data.

Preparation of Ketal Acid 42. The following modification of the previously described procedure[12] was used to prepare the unsaturated ester **41**. A cold (−5 °C) mixture of 1.89 g (7.00 mmol) of the ester **40** and 10 g of liquid 1,3-butadiene was sealed in an autoclave and heated to 130–140 °C for 17 h. After the mixture had cooled to 25 °C, it was dissolved in 100 mL of $CHCl_3$ and diluted with 50 mL of Et_2O and 50 mL of pentane. The resulting mixture was filtered, and the filtrate was concentrated to leave 15.33 g of yellow liquid. This mixture was chromatographed on basic Al_2O_3 diethyl ether–pentane (1:4, v/v) as the eluent. Fractions containing 1.76 g (80%) of the ester **41** were separated as a yellow liquid that solidified on standing, mp 76–77 °C [lit.[12] mp 75.5–77 °C]. This product was identified with previously described[12] material by comparison of IR and NMR spectral data.

A solution of 1.419 g (4.49 mmol) of the ester **41** and 25 mL of aqueous 4 M NaOH in 25 mL of MeOH was refluxed for 24 h and then diluted with 100 mL of H_2O and extracted with Et_2O to separate 61 mg of neutral material. The aqueous phase was mixed with 200 g of ice and 500 mL of CH_2Cl_2 and then acidified (pH 1) by dropwise addition of cold aqueous 1 M HCl. The CH_2Cl_2 layer was separated **immediately**, and the cold aqueous phase was extracted with an additional portion of CH_2Cl_2. After the combined CH_2Cl_2 solutions had been washed with aqueous NaCl, dried, and concentrated, a solution of the residue in warm $CHCl_3$ was diluted with hexane to precipitate 1.31 g (96%) of the ketal acid **42** as a pale-cream solid, mp 137–137.8 °C dec. Recrystallization from either chloroform–hexane or THF–hexane afforded the acid **42** as small white plates: mp 138.5–140 °C dec; IR (CCl_4) 1733, 1708 (shoulder) cm^{-1} (carboxyl C=O); UV max (95% EtOH), 213 nm (ϵ 6220), 221 (6120), 226 (5980), 283.5 (2440), 290 (2150); NMR ($CDCl_3$) δ 11.32 (1 H, br, OH), 6.6–7.3 (3 H, m, aryl CH), 5.67 (2 H, br, vinyl CH), 3.8–4.5 (5 H, m, ketal CH_2 and benzylic CH), 3.78 (3 H, s, OCH_3), 1.8–3.0 (4 H, m, CH_2); mass spectrum, *m/e* (rel intensity) 302 (M^+, 8), 259 (18), 258 (100), 213 (57), 204 (17), 197 (25), 196 (59), 195 (63).

Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.53; H, 6.05.

Preparation of Iodo Lactone 43. The crude ketal acid **42** (4.04 g) obtained by the previously described saponification of 4.462 g (14.1 mmol) of the ester **41** was dissolved in a mixture of 8.40 g (100 mmol) of $NaHCO_3$, 25 mL of H_2O, and 75 mL of THF, and then a mixture of 2.81 g (16.9 mmol) of KI, 10.74 g (42.3 mmol) of I_2, and 75 mL of H_2O was added. After the resulting mixture had been stirred (N_2 atmosphere) for 24 h at 25 °C, it was partitioned between Et_2O and aqueous $Na_2S_2O_3$. The colorless Et_2O phase was washed with aqueous $NaHCO_3$, dried, and concentrated to leave 3.44 g of the crude iodo lactone **43**, mp 149.5–150 °C dec. Extraction of the various aqueous solutions with $CHCl_3$ separated an additional 1.31 g (total yield 4.75 g or 79%) of the crude iodo lactone **43**, mp 157–158 °C dec. The combined crude samples of the iodo lactone were recrystallized from a chloroform–hexane mixture to give the pure iodo lactone **43** as a colorless solid, mp 162.9–163.5 °C dec; IR ($CHCl_3$) 1777 cm^{-1} (γ-lactone C=O); UV max (95% EtOH) 220 nm (ϵ 9430), 255 (shoulder, 9340), 281 (3040), 288.5 (2610); NMR ($CDCl_3$) δ 6.8–7.2 (3 H, m, aryl CH), 5.07 (1 H, d, J = 5 Hz, further splitting not resolved, CHO), 3.0–4.6 (9 H, m, aliphatic CH including a CH_3O singlet at 3.82), 2.0–2.6 (4 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 428 (M^+, 16), 214 (64), 210 (47), 195 (22), 160 (100), 155 (84), 44 (36).

Anal. Calcd for $C_{17}H_{17}IO_5$: C, 47.67; H, 4.00; I, 29.65. Found: C, 47.69; H, 4.03; I, 29.58.

Preparation of Ketal Lactone 44. The previously described[26] reduction of *n*-Bu_3SnCl with $LiAlH_4$ in Et_2O yielded 82% of *n*-Bu_3SnH as a colorless liquid: bp 72–75 °C (0.2 mm); n^{25}_D 1.4707 [lit.[26] bp 76–81 °C (0.7–0.9 mm)]. A solution of 1.85 g (4.32 mmol) of the iodo lactone **43**, 1.40 g (4.81 mmol) of *n*-Bu_3SnH, and 50 mg of AIBN (azoisobutyronitrile) in 30 mL of PhH and 30 mL of THF was refluxed under an N_2 atmosphere for 12 h and then cooled and concentrated. The residual solid was washed with hexane to leave 1.28 g (98%) of the lactone **44**, mp 200.5–203 °C. Recrystallization from a chloroform–hexane mixture separated the lactone **44** as colorless prisms, mp 203.5–204 °C; IR ($CHCl_3$) 1770 cm^{-1} (γ-lactone C=O); UV max (95% EtOH), 220 nm (ϵ 6520), 282 (2440), 288.5 (2220); NMR ($CDCl_3$) δ 6.7–7.4 (3 H, m, aryl CH), 4.6–5.0 (1 H, m, OCH), 3.9–4.4 (4 H, m, ketal OCH_2), 3.82 (3 H, s, OCH_3), 3.53 (1 H, t, J = 7 Hz, benzylic CH), 1.4–2.7 (6 H, m, CH_2); mass spectrum, *m/e* (rel intensity) 303 (22), 302

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(M^+, 100), 258 (24), 214 (39), 213 (87), 187 (38), 174 (24), 173 (22), 115 (23).

Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.52; H, 6.04.

Conversion of Lactone 44 to Methoxy Ketone 48. A solution of 404 mg (3.2 mmol) of dimethyl methylphosphonate in 10 mL of THF was added, dropwise and with stirring during 10 min, to a cold (-78 °C) solution of 2.4 mmol of *n*-BuLi in 1.7 mL of hexane. After the resulting suspension 11 had been stirred at -78 °C for 15 min, a solution of 282 mg (0.93 mmol) of the lactone **44** in 60 mL of THF was added, dropwise and with stirring during 45 min. The resulting cold suspension was warmed to 0 °C, and the resultant colorless solution was partitioned between $CHCl_3$ and aqueous HCl. After the organic phase had been washed with aqueous NaCl, it was dried and concentrated to leave a yellow semisolid containing (IR and NMR analysis) a mixture of the starting lactone **44** and the phosphonate **45**. Consequently, a solution of the crude product in 10 mL of DME was added a second time to a cold (-78 °C) slurry of 2.4 mmol of $LiCH_2P(O)(OCH_3)_2$ in 1.7 mL of hexane and 10 mL of DME. After the resulting mixture had been warmed to 0 °C during 3 h, it was subjected to the previously described isolation procedure to separate a pale yellow semisolid. The crude product was chromatographed on silica gel to separate 45 mg of the starting lactone **44** in early fractions eluted with Et_2O. Subsequent fractions, eluted with EtOAc, contained 315 mg of the crude phosphonate **45** as a colorless solid. Recrystallization of the phosphonate **45** from a chloroform-hexane mixture afforded 257 mg (68%) of the phosphonate **45** as colorless prisms: mp 177.5-178 °C; IR ($CHCl_3$) 3400 (OH), 1710 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 6.7-7.4 (3 H, m, aryl CH), 3.7-4.7 (13 H, m, ketal CH_2O and CH_3O), 1.0-3.6 (10 H, aliphatic CH); mass spectrum, *m/e* (rel intensity) 409 (1), 275 (45), 258 (33), 257 (56), 214 (22), 213 (100), 195 (30), 151 (85), 124 (25), 109 (35), 85 (24), 83 (39), 43 (31), 41 (20). This product was oxidized without further purification or characterization.

A cold (0-5 °C) solution of 240 mg (0.56 mmol) of the crude phosphonate **45** in 75 mL of acetone was treated with 0.20 mL of aqueous 8 N H_2CrO_4 (Jones reagent). After the resulting cold solution had been stirred for 15 min, it was partitioned between H_2O and $CHCl_3$. The organic layer was washed with aqueous NaCl, dried, and concentrated to leave 263 mg of viscous yellow liquid. This crude product was chromatographed on silica gel with an EtOAc-$CHCl_3$ eluent to separate 208 mg of the phosphonate **46** as a yellow liquid: IR ($CHCl_3$) 1710 cm^{-1} (C=O); mass spectrum, *m/e* (rel intensity) 424 (M^+, 10), 362 (39), 273 (44), 229 (32), 151 (100), 124 (34), 109 (43), 43 (29).

Anal. Calcd for $C_{20}H_{25}O_8P$: M_r, 424.1280. Found: M_r, 424.1235.

A mixture of 166 mg (0.39 mmol) of the phosphonate **46**, 90 mg (0.85 mmol) of Na_2CO_3, and 5 mL of MeOH was stirred at 25 °C. TLC analysis (silica gel coating with an Et_2O eluent) indicated that both the starting phosphonate **46** (R_f 0.04) and the methoxy ketone product **48** (R_f 0.54) were present after 18 h. Therefore this mixture was refluxed for 2 h and then concentrated under reduced pressure. The residual solid was extracted with $CHCl_3$, and the $CHCl_3$ extract was concentrated to leave 159 mg of amber liquid. This material, which solidified on standing, was chromatographed on silica gel with an Et_2O eluent to separate 126 mg of the crude methoxy ketone **48** as a yellow solid. Recrystallization from a $CHCl_3$-Et_2O-hexane mixture separated 101 mg (78%) of the methoxy ketone **48** as colorless needles: mp 129-130 °C; IR (CCl_4) 1745 cm^{-1} (cyclopentanone C=O); ^1H NMR (CCl_4) δ 6.6-7.1 (3 H, m, aryl CH), 3.85-4.3 (4 H, m, ketal CH_2O), 3.77 (3 H, s, $ArOCH_3$), 2.5-3.7 (4 H, m, aliphatic CH including a CH_3O singlet at 3.15), 2.3-2.4 (2 H, br, CH_2CO), 0.8-2.3 (6 H, m, aliphatic CH); mass spectrum, *m/e* (rel intensity) 330 (M^+, 17), 105 (91), 91 (31), 77 (37), 41 (100), 40 (31); UV max (95% EtOH), 219 nm (ϵ 7660), 290 (2400).

Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71; M_r, 330.1461. Found: C, 69.05; H, 6.73; M_r, 330.1473 (mass spectrum).

Registry No. **1**, 73274-32-5; **2**, 70562-48-0; **3**, 71370-30-4; **4**, 84211-62-1; **5**, 85319-15-9; **6**, 497-38-1; **8**, 5724-61-8; **9a**, 37435-80-6; **9b**, 85354-06-9; **10a**, 85319-16-0; **10b**, 85319-17-1; **12**, 85319-18-2; **13**, 85319-19-3; **14**, 85319-20-6; **15**, 85319-21-7; **17**, 75359-72-7; **18a**, 6493-80-7; **18b**, 16646-42-7; **19**, 85319-22-8; **20**, 64326-18-7; **21**, 85319-23-9; **22** (isomer 1), 85319-24-0; **22** (isomer 2), 85319-25-1; **23a**, 85319-26-2; **23b**, 85319-27-3; **24**, 85319-28-4; **25**, 85319-29-5; **26a**, 85319-30-8; **26b**, 85319-31-9; **27** (isomer 1), 85319-32-0; **27** (isomer 2), 85319-33-1; **28**, 85319-34-2; **31a**, 85319-35-3; **31a** 2,4-DNP, 85319-36-4; **31b**, 85404-35-9; **32**, 85319-37-5; **33**, 85319-38-6; **34**, 85319-39-7; **36**, 85319-40-0; **37**, 62015-84-3; **38**, 62015-87-6; **40**, 62015-88-7; **41**, 62015-92-3; **42**, 85319-41-1; **43**, 85319-42-2; **44**, 85319-43-3; **45**, 85319-44-4; **46**, 85319-45-5; **48**, 85319-46-6; **49**, 85319-47-7; **50**, 85319-48-8; CH=CHCH=CH_2, 106-99-0; methyl methacrylate, 80-62-6; 3,5-dimethyl-2-cyclohexen-1-one, 1123-09-7.

Supplementary Material Available: Descriptions of determination of crystal structures for the adduct **31a** and the cyclobutane **32**, including tables of atomic coordinates for each compound (8 pages). Ordering information is given on any current masthead page.

Enones with Strained Double Bonds. 9. The 2-Phenylbicyclo[3.3.1]non-1-en-3-one System[1]

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Reaction of the bromo ketone **2** with Et_3N formed the phenyl-substituted bicyclo[3.3.1]nonenone **1c** that was stable when protected from oxygen, water, or other nucleophiles. The enone **1c** added MeOH to form the methoxy ketone **4** and reacted slowly with Et_3N at 100 °C to form the reduced ketone **3**. The enone **1c** reacted slowly with butadiene at 100 °C to form a mixture of the cycloadducts **13**, **15**, and **16**. Reaction of the enone **1c** with oxygen formed a solid mixture of peroxides (presumably **9** and **11**). These peroxides reacted with Et_3N to form the diol **5** and underwent thermal rearrangement at 50 °C to form the triketone **6**. The reactions with O_2 and with butadiene suggest that the enone **1c** tends to react as a diradical species.

Our previous study[2] of bicyclo[3.3.1]nonenone bridgehead enones **1** indicated that the ready reaction of the parent enone **1a** with itself to form 2 + 2 cycloadducts could be markedly retarded by placing a substituent at the

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