(15), 77 (26), 69 (10), 67 (31), 55 (25), 43 (12), 41 (20) (calcd for $C_{18}H_{22}SO_3$, 318.1289; found, 318.1285); ^{13}C NMR (PhH-d_6) 211.0, 136.8, 136.7, 134.0, 131.2, 128.8, 126.7, 75.8, 47.7, 38.1, 28.5, 25.6, 24.2, 23.1, 22.5, 15.8 (q). Anal. Calcd for $C_{18}H_{22}SO_3$: C, 67.89; H, 6.96; S, 10.07. Found: C, 67.74; H, 6.98; S, 10.07.

The mother liquor provided a second crop of crystals, and the resulting mother liquor showed a 59:35 *E*:*Z* ratio. Partial spectra: ^1H NMR (270 MHz, $CDCl_3$) 5.83 (bs, 0.06 H), 5.62 (bs, 0.59 H), 5.32 (bs, 0.35 H), 1.44 (s), 1.26 (s), 1.11 (s); ^{13}C NMR (67.9 MHz, PhH-d_6) 22.5 (q), 21.1 (q), 15.8 (q).

Method B from 20. To a stirred solution of acetate **20** (85.1 mg, 0.23 mmol) in 1.1 mL of dry Me_2SO (previously deoxygenated by flushing with argon) at 25 °C under argon was cautiously added NaH (5.2 mg, 0.22 mmol). The mixture was stirred for 2 h to give a clear, orange-yellow solution. Catalyst **29** (12.8 mg, 0.014 mmol) was added, and the mixture was heated to 130 °C over 15 min. After 45 min at 130 °C the deep red-brown solution was cooled to 25 °C, concentrated in vacuo, and filtered through Florisil (5 × 0.5 cm) with EtOAc (20 mL). Concentration in vacuo and preparative TLC purification, using three elutions with 20% acetone in hexane (v/v), yielded the same product as above (35.8 mg, 52%) as an off-white solid, the physical and spectral characteristics of which were identical with those of the material obtained from reaction of the enol ether. The progress of the reaction can be followed by analytical TLC or NMR, and it clearly proceeds through the intermediacy of the enol ether **21**.

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Palladium-Catalyzed 1,3-Oxygen-to-Carbon Alkyl Shifts. A Cyclopentanone Synthesis

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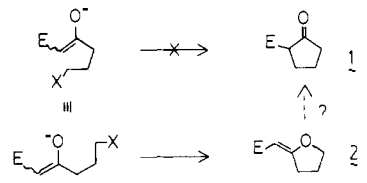
Abstract: A cyclopentanone synthesis emerges from the Pd(0)-catalyzed isomerization of 5-vinyl-2-alkylidenetetrahydrofurans. Four routes into such species were developed. First, cyclization of β-keto esters leads to O- rather than C-alkylation. Second, olefination of 4-vinyl lactones produced such substrates. The availability of such vinyl lactones from carbohydrates translates into a chiral synthesis of cyclopentanones. Third, 1-(arylthio)cyclopropanecarboxaldehyde served as a conjunctive reagent to convert ketones into the requisite substrates. Fourth, methyl 6-oxo-2-hexynoate converts vinyl organometallics into 5-vinyl-2-alkylidenetetrahydrofurans. In connection with this last conjunctive reagent, the intramolecular addition of a nucleophile to an ynoate is considered. The ability to direct the rearrangement to cyclopentanone or cycloheptenone formation [i.e., Pd(0)-catalyzed [1.3] vs. [3.3] rearrangement] is considered. The application of this method to the synthesis of steroids and prostaglandins is presented.

The discovery of natural products that contain five-membered rings has flourished in the last two decades. While prostaglandins and their metabolic relatives and the rethrolones, representatives of monocyclic systems, provided a major stimulus, polycondensed cyclopentanoids such as the hirsutanes,[1] capnellanes,[2] pentalanes,[3] zizaanes,[4] isocomanes,[5] and [3.3.3]propellanes[6] provided an even greater challenge. Natural products that contain one five-membered ring as part of a more complex ring system are numerous. The vetivanes[7] and steroids, which fall into this category, have stimulated much innovative work.

Among the most strategically innovative approaches have been the use of the intramolecular Alder ene reaction,[8] the vinylcyclopropane–cyclopentene rearrangement,[9] and photochemical cycloadditions.[10] Of the more classical approaches, one of the most useful would be intramolecular alkylation, as shown in eq 1. The thwarting of this approach due to the preference for O-



(1)

rather than C-alkylation derives from stereoelectronic considerations.[11,12] The particular flexibility associated with a β-keto ester (i.e., **1** when E = CO_2CH_3) for structural elaboration imparts special importance to devise a route to achieve this transformation.[13] Since bond-energy considerations suggest that **1** is more

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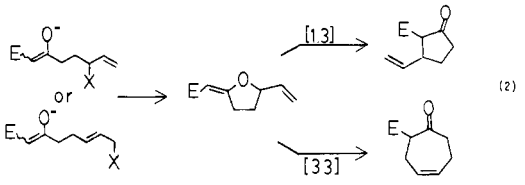
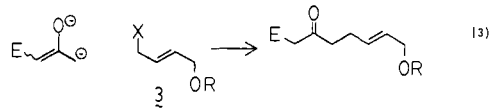
stable than **2**, could a pathway be found to effect an isomerization of **2** → **1**? We considered this question in the context of an allyl derivative as the electrophile (eq 2). In the previous paper,[14] we



(2)

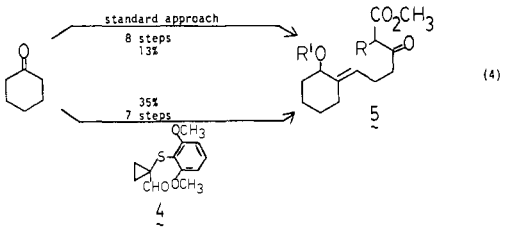
discussed the basic process and the fact that a reordering of reactivity arises by use of transition-metal catalysts. In this paper, we wish to consider the synthetic implications, which include (1) general approaches to 2-alkylidene-5-vinyltetrahydrofurans, (2) regiochemical control of the isomerization, and (3) stereochemistry of the allyl unit during the isomerization.[15]

Synthesis of 2-Alkylidene-5-vinyltetrahydrofurans via 1-(Arylthio)cyclopropanecarboxaldehyde as a Conjunctive Reagent. The conceptually simplest approach is the direct intramolecular cyclization of the β-keto ester as represented in eq 2. To the extent that allyl derivatives such as **3** are accessible, direct alkylation



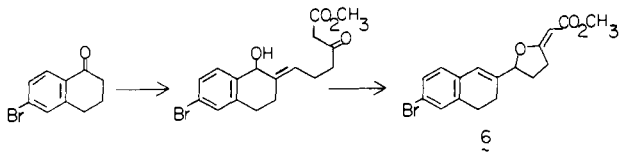
(3)

of dianions[16] serves as an excellent entry (eq 3). Difficulties in the synthesis of cyclic analogues of **3** led to the evolution of a new conjunctive reagent, **4**, whose advantages are clearly illustrated by the comparison of eq 4.[17] Using a standard approach to create

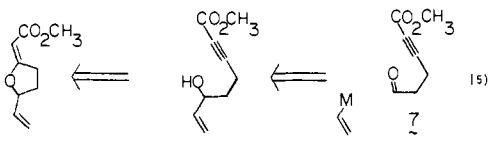


(4)

an alkylating agent of type **3** from cyclohexanone and then performing the dianion alkylation led to **5** after eight steps in 13% overall yield. Utilizing **4** allows a slightly shorter sequence, with the overall yield almost tripling. For the present purposes, this approach focused on the synthesis of **6** as an entry into modified steroids.[17]



Synthesis of 2-Alkylidene-5-vinyltetrahydrofurans via Methyl 6-Oxohex-2-ynoate as a Conjugative Reagent. Equation 5 represents an alternative retrosynthetic analysis and suggests methyl



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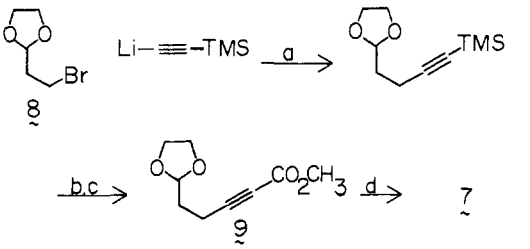
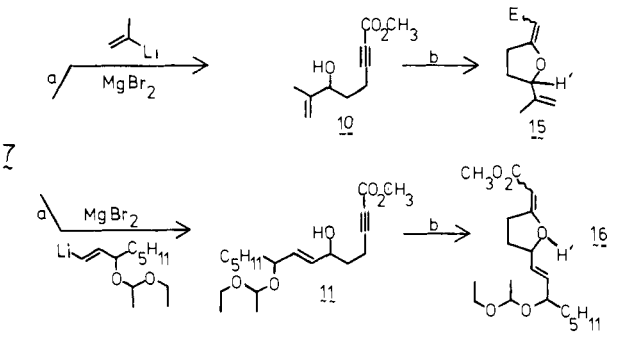
Scheme I. Synthesis of Conjunctive Reagent, Methyl 6-Oxohex-2-ynoate



[a] THF, HMPA, −78 °C. [b] KOH, CH_3OH. [c] n-C_4H_9Li, THF, then $ClCO_2CH_3$. [d] 0.5 N H_2SO_4, THF, H_2O, reflux.

Scheme II. Methyl 6-Oxohex-2-ynoate as Conjunctive Reagent

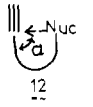


[a] THF, −78 °C. [b] $PhSO_2Na$, CH_3OH, 30–50 °C.

6-oxohex-2-ynoate (**7**)[18] as another type of conjunctive reagent for the synthesis of 2-alkylidene-5-vinyltetrahydrofurans. Scheme I illustrates the ready availability of **7** in 36% overall yield from bromide **8**[19] which, in turn, arises from treatment of acrolein with anhydrous HBr in ethylene glycol. An attempt to use the anion of methyl propiolate[20] with **8** to give **9** directly failed. Use of the dianion of propiolic acid[21] with **8** followed by esterification with DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and methyl iodide gave **9** in only 25% yield. During the course of our work, an alternate synthesis of **7** in 11–13% overall yield which utilized the less economical 1-hydroxy-4-pentyne as the starting material appeared.[18] The acetal **9** being perfectly stable for months at −6 °C proved to be a convenient storage point. For subsequent reactions, the aldehyde **7** normally contained 3–8% of acetal **9**. The ease of removal of the latter after addition of a Grignard reagent led us to utilize this mixture.

Vinyllithium reagents appear to lack chemoselectivity. On the other hand, conversion of the organolithium reagent to an organomagnesium reagent by addition of magnesium bromide (either as the solid or as a standard ether solution) led to selective addition to the aldehyde to give **10** and **11** (see Scheme II). Since chromatographic purification of the alcohol at best did not affect the subsequent cyclization and at worst caused substantial decomposition and since we wished to minimize the manipulation of any intermediates, the crude alcohol was directly cyclized.

The cyclization represents an example of a 5-exo-digonal ring closure.[22-25] The preferred angle (α) of approach (cf. **12**) to



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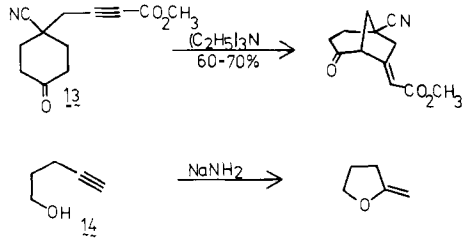
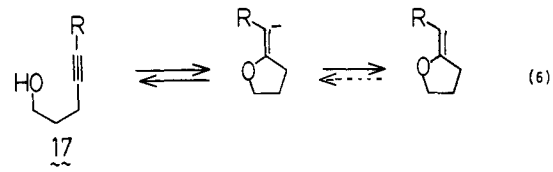
acetylenes has been controversial. While an angle of 120° had been speculated, no experimental support exists, and theoretical arguments refute such a suggestion. Such an angle is unattainable for **13**[25] and **14**[24a] and yet cyclization occurs. The latter is a



particularly good model for our case. Surprisingly, treatment of **10** with a wide variety of bases either failed or gave very little **15**. For direct cyclization, use of 0.2 equiv of sodamide in toluene at 90 °C or simply stirring with Woelm alumina in methylene chloride at 25 °C proved most efficient, although the yields were only 30% and 39%, respectively.

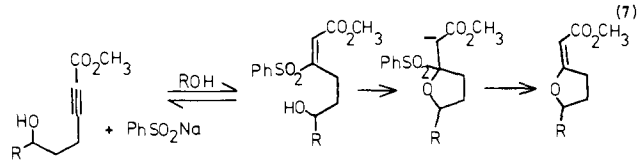
Two rationales may be proffered. First, the question of angle of approach may be considered. If the original suggestion of an angle of 120° has validity, this process is disfavored. However, such a rationale is hard to accept based upon the cases cited above (i.e., **13** and **14**). In very recent work, examples related to **14** cyclized in >80% yields.[24b] A second explanation considers the effect of the carbomethoxy group on the reversibility of the reaction (eq 6) When only a catalytic amount of a strong base is em-



(6)

ployed, as in the case of **14**, the initial carbanion is rapidly and essentially irreversibly protonated. When R = CO_2CH_3 in **17**, protonation of the initial enolate is slowed and may then become reversible. Such a situation would allow competing decomposition pathways. Weak base simply gave no reaction.

For circumvention of the feared problems, the use of benzenesulfinate anion as a nucleophilic trigger was envisioned (eq 7).



(7)

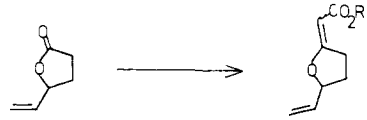
18

Conjugate addition of the sulfinate anion converts a 5-exo-digonal process into a favorable 5-exo-trigonal process.[12] Furthermore, the enolate **18** would be expected to preferentially expel the sulfinate anion to give product rather than alkoxide which returns it to starting material. Indeed, treatment of pure samples of **10** and **11** with 1 equiv of sodium benzenesulfinate in methanol at 30 °C leads smoothly to the desired alkylidenetetrahydrofurans **15** and **16** in 80% and 98% yields, respectively (overall yields from **7** without purifying any intermediates were 52% and 54%, respectively). In the case of **11**, the cyclization proceeded smoothly at 30 °C on a purified sample, but required a slightly higher temperature (45 °C) for longer times with the crude sample.

The assignment of the *E,Z* isomers is based on spectral arguments which parallel those presented for all of the previous alkylidenetetrahydrofurans. As before, the *Z* isomers were found to undergo facile thermal isomerization to the thermodynamically more stable *E* isomers. Therefore, spectra and reactions of *Z* isomers were obtained as soon as possible after isolation. The allylic methylene protons of (*Z*)-**15** are found as a pseudo triplet at δ 2.74 which 270-MHz ^{1}H NMR reveals to be a d of d of d (J = 9.4, 7.0, 1.0 Hz). The corresponding protons of (*E*)-**15** are deshielded by their cis relationship to the carbonyl group of the ester, δ 3.28 (dddd, J = 18.5, 9.2, 5.0, 1.6 Hz) and 3.02 (dtd, J = 18.5, 8.8, 1.6 Hz). A major shift is also observed in the opposite direction for the methine of the tetrahydrofuran ring (H′). In (*Z*)-**15** H′ is deshielded (δ 5.00) by the carbonyl of the ester, while it is found upfield (δ 4.79) in (*E*)-**15**.

The analysis of compound **16** is complicated by the mixture of four diastereomers present in each olefin isomer. The 270-MHz ^{1}H NMR shows the allylic methylene protons of (*Z*)-**16** as a pseudotriplet (δ 2.73) while the cis carbonyl group present in (*E*)-**16** deshields and resolves these protons (δ 3.27 and 3.00). The ring methine proton is deshielded in (*Z*)-**16** (δ 5.06) but is found upfield in (*E*)-**16** (δ 4.83). The diastereomeric mixture is most evident in the 50.1-MHz ^{13}C NMR spectra, but the resolution of all peaks into four signals is not consistently observed (see Experimental Section). Final proof of any stereoselectivity in the aldehyde-addition step must await the Pd-catalyzed rearrangement and the removal of the ethoxy-ethoxy protecting group.

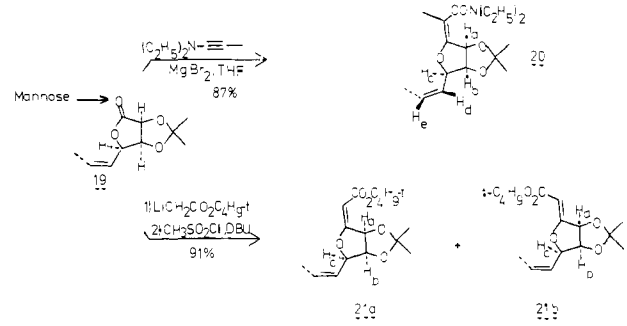
Synthesis of 2-Alkylidene-5-vinyltetrahydrofurans from Lactones. An attractive approach to the requisite substrates envisions an olefination of a vinyl lactone (eq 8).[26] Such an approach is



(8)

particularly attractive because of the easy accessibility of such vinyl lactones from carbohydrates.[27] Such starting materials confer special significance on this methodology as a route that can control absolute as well as relative stereochemistry. Thus, we focused our efforts on the olefination of a vinyl lactone from a carbohydrate.

Lactone **19**, available from mannose as previously described,[27] resisted all attempts to react with Wittig or Emmons–Wadsworth–Horner reagents. On the other hand, reaction of 1-(diethylamino)propyne and anhydrous magnesium bromide[28] produces the conjugated amide **20** in 87% yield as a single stereoisomer. The *E* configuration is evidenced by the abnormally



downfield shift of H_a (δ 5.28) and the homoallylic coupling of 0.6 Hz between H_a and the vinyl methyl. Also the examples in the literature indicate the reaction to be highly stereoselective in this manner. The IR absorption at 1605 cm^{-1} is broad and strong, presumably caused by both the conjugated amide and the enol ether. The relative stereochemistry of the acetonide and the

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Table I. Pd-Catalyzed Rearrangement of 20

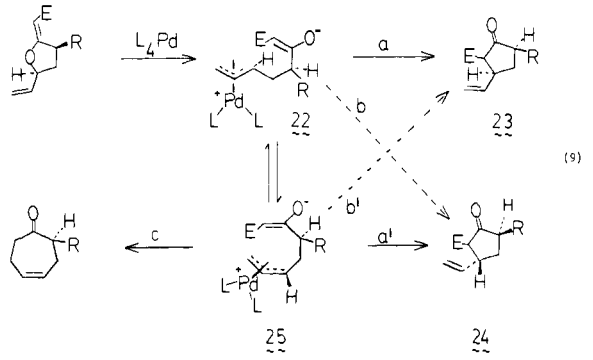
entry	conditions	product, % yield 20	26	27
1[a,b]	6% $(dppe)_2Pd$, Me_2SO, 120 °C, 2 h		35	27
2[c]	6% $(Ph_3P)_4Pd$, Me_2SO, 130 °C, 47 h	73	20	6
3[a]	6% $(dppe)_2Pd$ dioxane, 90 °C, 1 h		93	

[a] Yields determined by TLC isolation. [b] In addition 11% of 28 and 10% of 29 isolated. [c] Yield determined by HPLC.

1-propenyl substituent is dictated by the method of synthesis and supported by a value for J_{bc} of 4.1 Hz. The cis nature of the 1-propenyl group is shown by the 11.0-Hz coupling constant between the olefinic protons H_d and H_e and the 13.5-ppm chemical shift of the vinyl methyl group in the ^{13}C NMR spectrum.

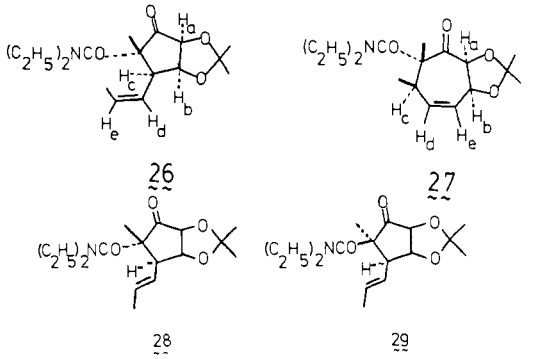
A two-step procedure involves initial addition of the lithium enolate of *tert*-butyl acetate to the carbonyl group of **19** at −78 °C in THF and isolation of the stable β-hydroxy ester.[29] Subsequent treatment with methanesulfonyl chloride in the presence of DBU yielded the desired alkylidenetetrahydrofuran **21** in 91% yield as an easily separable mixture of olefin isomers (*E*/*Z*:2/1). The coupling constants of interest, J_{bc}, were easily discernible in the 270-MHz ^1H NMR (E, 4.0 Hz; *Z*, 3.7 Hz). It is known that compounds with the opposite relative stereochemistry exhibit J_{bc} values of approximately 0 Hz.[27] The assignment of the olefin stereochemistry of **21** is made on the basis of the 270-MHz ^1H NMR data and thermodynamics. The minor isomer rearranges to the major isomer upon heating and, on the basis of previous observations, would be assigned the *Z* geometry. Furthermore, it possesses an H_a (δ 5.12) upfield relative to the major *E* isomer (δ 5.71). This is a consequence of the deshielding effect of the carbonyl group of the diethyl amide on cis substituents. Both isomers show strong IR bands at 1700 and 1655 cm^{-1} for the conjugated ester and enol ether.

Formation of Cyclopentanones. With the availability of the requisite substrates from a wide variety of approaches, attention focused on the rearrangement to cyclopentanones. For synthetic applications, several questions of stereochemistry remain to be established. Assuming the ionization generates **22** (see Discussion), the mechanism of its collapse determines its stereochemical fate. If collapse involves backside displacement as has been established for the intermolecular processes (eq 9, path a),[30] formation of **23**



results. On the other hand, initial coordination of the oxallyl unit (the enolate) with palladium followed by reductive elimination forms **24** (eq 9, path b).[31] Furthermore, if syn–anti interconversion (i.e., **22** ⇄ **25**) competes with cyclization, a mixture of stereoisomers would likely result. Synthetically, conversion of the stereochemistry of the starting material into the stereochemistry of the product (i.e., a stereospecific reaction) would be most useful.

Substrates **20** and **21** offer an opportunity to examine this question. Initial attention focused on amide **20** with the results summarized in Table I. In the first reaction (Table I, entry 1), four products were isolated after TLC purification: **26**–**29**.



However, repetition of the reaction in Me_2SO-d_6 with NMR monitoring revealed no evidence for **28** and **29**. Furthermore, these products were absent in the product mixtures from the other rearrangements. At present, we conclude that **28** and **29** are artifacts of that particular run and/or reaction or isolation conditions. Most striking is the isolation of cycloheptenone **27**—a type of product that heretofore had not been seen. As eq 9 reveals, such a product must arise from the intermediate of syn–anti interconversion, **25**, since formation of a seven-membered ring from **22** would place a trans double bond in a seven-membered ring. Further elaboration of this point is reserved for the Discussion section. Suffice it to say at this point, rational manipulation of reaction conditions allows control of the product distribution. For example, use of triphenylphosphine as a ligand increases the ratio of five- to seven-membered rings from 1.3 to 3.3 (Table I, entry 2) under otherwise similar conditions. Most dramatically, change of solvent totally reorients the reaction toward exclusive formation of the cyclopentanone (Table I, entry 3).

Compounds **26**–**29** were isolated pure and fully characterized. The cyclopentanone **26** shows typical carbonyl bands at 1750 and 1620 cm^{-1} consistent for the ketone and tertiary amide. The 270-MHz ^1H NMR spectrum reveals all of the protons: δ 1.11 (t, 6 H, *J* = 8.0 Hz), 1.34 (s, 3 H), 1.39 (s, 3 H), 1.46 (s, 3 H), 1.68 (dd, 3 H, *J* = 7.0, 2.0 Hz), 3.17 (m, 2 H), 3.35 (m, 2 H), 3.73 (ddd, 1 H, *J* = 10.5, 4.9, 0.8 Hz H_c), 4.73 (m, 2 H, H_a, H_b), 5.48 (ddq, 1 H, *J* = 11.0, 10.5, 2.0 Hz, H_d), 5.82 (dqd, 1 H, *J* = 11.0, 7.0, 0.8 Hz, H_e). The 11.0-Hz value for J_{de} and the ^{13}C shift of δ 13.3 for the vinyl methyl carbon confirm the presence of the (*Z*)-1-propenyl group. The substantial value for J_{bc} (4.9 Hz) demonstrates the retention of the cis relative stereochemistry for the 1-propenyl group and the acetonide from that of the starting material.

The assignment of stereochemistry at the quaternary carbon is indicated by the deshielding effect of the carbonyl group of the diethylamide on H_c (δ 3.73) due to their cis relationship and the upfield shift of the angular methyl carbon atom (δ 17.8) due to "steric compression" (the γ effect) by the *cis*-1-propenyl substituent. The *S* configuration is further supported by the results of a nuclear Overhauser enhancement (NOE) experiment.[32] Mild irradiation of the angular methyl group at a variety of power levels resulted in a maximum enhancement of the signal for H_d by 16.5%. The strong distance relationship of this effect assures that the angular methyl is cis to the 1-propenyl substituent.

Cycloheptenone **27** distinguished itself by its 1725- and 1620-cm^{-1} IR absorptions for both the ketone and tertiary amide carbonyl groups. The (*Z*)-olefin geometry is shown by the 10.5-Hz coupling constant between H_d and H_e. Irradiation at δ 3.54 (H_c) effects the following perturbations: (1) the collapse of the allylic

(29) Duggan, A. J.; Adams, M. A.; Brynes, P. J.; Meinwald, J. *Tetrahedron Lett.* **1978**, 4323.

(30) Trost, B. M. *Tetrahedron* **1977**, *33*, 2615; *Acc. Chem. Res.* **1980**, *12*, 385.

(31) For oxallylpalladium complexes, see: Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011. Ito, Y.; Aoyama, H.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 4519 and earlier references. Cf.: Shimizu, I.; Yamada, T.; Tsuji, J. *Tetrahedron Lett.* **1980**, *21*, 3199. Chujo, Y.; Nishi, S.; Tawara, K.; Saegusa, T. *J. Am. Chem. Soc.* **1980**, *102*, 6381.

(32) Noggle, J. H.; Shirmer, R. E. "The Nuclear Overhauser Effect: Chemical Applications"; Academic Press: New York, 1971.

Table II. Pd-Catalyzed Rearrangement of (*E*)- and (*Z*)-**21**

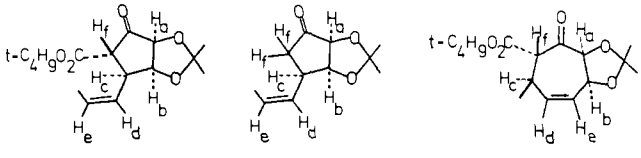
entry	21 *E* or *Z* isomer	conditions	product, % yield 30[a]	31	32
1[b]	*E*	6% $(dppe)_2Pd$, Me_2SO, 100 °C, 10 min			64
2[b]	*Z*	6% $(Ph_3P)_4Pd$, Me_2SO, 60 °C, 7 h		35	50
3[c]	*E*	6% $(Ph_3P)_4Pd$, dioxane, 100 °C, 5 h	5	38	28
4[c,d]	*Z*	3% PS -Pd, dioxane, 100 °C, 10 h	11[d] 17[c]	75[d] 79[c]	5[d] 4[c]
5[c,d]	*E*	3%, PS -Pd, $PhCH_3$, O, N-bis,[e] 100 °C 10 h	98[f]		2
6[b]	*E*	above, then Me_2SO, 70 °C		82	

[a] Exists as a mixture of keto and enol forms. [b] Isolated yield(s) after TLC purification. [c] Yield determined by HPLC. [d] Yield determined by NMR spectroscopy. [e] O, N-bis = O, *N*-bis(trimethylsilyl) acetamide. [f] Formed as the enol silyl ether of **30**.

methyl group protons at δ 1.19 (d, J = 6.8 Hz) to a singlet, (2) the collapse of H_d (ddd, J = 10.5, 6.8, 2.0 Hz) to a d of d (J = 10.5, 2.0 Hz), (3) the collapse of H_e (dt, J = 10.5, 1.5 Hz) to a d of d (J = 10.5, 1.5 Hz), and (4) a sharpening of the multiplet corresponding to H_a and H_b. Subsequent irradiation of these last protons (δ 5.14) collapsed H_c (quintet of t, J = 6.8, 1.4 Hz) to a quintet of d (J = 6.8, 1.4 Hz).

The extraordinary homoallylic coupling of H_b and H_c (J_{bc} = 1.3 Hz) requires the allylic methyl group to be cis to the acetonide so that H_b and H_c can both be oriented parallel with the p orbitals of the olefin for maximum transmission of spin information.[33] The abnormal downfield shift of H_c (δ 3.54) indicates that it is deshielded by a cis relationship to the diethylamide carbonyl. In the ^{13}C NMR spectrum, the allylic methyl and angular methyl groups appear to be shielded by "steric compression" (the γ effect) and absorb at δ 16.5 and 13.5, respectively. All of these spectral arguments are supported by the results of a single-crystal X-ray structural determination,[34] which clearly shows that the acetonide, the allylic methyl, and the angular methyl are all on the same face of the cycloheptenone ring. Bond distances and angles, as well as an ORTEP drawing of the molecule, may be found in the Appendix (supplementary material), which appears in the microfilm version of the Journal. The characterization of **28** and **29** appears in the Experimental Section.

A similar competition between five- and seven-membered ring products was observed in the rearrangement of **21** as summarized in Table II. The rearrangement of **21** occurred as fast as the catalyst dissolved to give a single product, the cycloheptenone **32** (Table II, entry 1). The much more rapid rearrangement of **21**

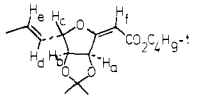


30[a] 31 32

compared to **20** is consistent with the oxidative addition being the rate-determining step and with the enolate of a β-keto ester being a better leaving group than the enolate of a β-keto amide. The relative leaving group abilities of the two systems may be correlated to the pK_A's in which the more acidic compound would be the better leaving group. An approximate difference of 2 pK_A units (β-keto ester 14.8 and β-keto amide 16.8)[35] may be estimated. Most significantly, consistent with eq 9, the exclusive formation of the seven-membered ring indicates syn–anti interconversion competes effectively with the initial C-alkylation.

This increased competition must be interpreted in terms of a decreased rate of C-alkylation, since a change in the intermediate enolate would not be expected to affect greatly the rate of syn–anti interconversion of the π-allyl moiety. The lower basicity of the β-keto ester enolate would explain the decreased rate of alkylation if a correlation between basicity and nucleophilicity of similar types of anions (β-dicarbonyl-like) were valid. Regardless, the selective formation of cycloheptenone **32**, rather than cyclopentanone (**30** or **31**), from the intermediate related to **25** in eq 9 is due to the bulky nucleophile's selectivity for the less-hindered alkylation pathway "c" via attack at the primary rather than secondary carbon.

In an attempt to force the intermediate to close to the cyclopentanone, the reaction with $(dppe)_2Pd$ was repeated in THF to inhibit syn–anti interconversion. These conditions (25 °C, 1 h) did not provide C-alkylation, and only the inverted O-alkylation product, **33**, was formed and isolated in 47% yield. It was found



33

to possess J_{bc} = 1.7 Hz, further supporting the ^1H NMR evidence for stereochemistry. This suggests that the rate-determining step (RDS) for $(dppe)_2Pd$ in THF solvent is the intramolecular C-alkylation.

Use of the more bulky $(Ph_3P)_4Pd$ catalyst in Me_2SO does increase cyclopentanone formation (Table II, entry 2), but the resultant mixture of products was not satisfactory. Further improvement in regiochemical control (Table II, entry 3) arises from use of dioxane as solvent, but still cycloheptenone **32** contaminated our desired cyclopentanones **30** and **31**. The employment of a newly developed, polymer-bound analogue to $(Ph_3P)_4Pd$, palladium(0) attached to 2% cross-linked porous polystyrene beads,[36] in dioxane would be expected to be even more selective than $(Ph_3P)_4Pd$.

While the polymeric system is difficult to define, it is known that 62% of the phenyl rings are phosphinylated and that the catalyst contains 3.76% (w/w) of palladium. Two of the possible bonding modes are depicted in Figure 1. Use of a portion of the catalyst (corresponding to 3 mol % palladium with respect to enol ether (*Z*)-**21**) in dioxane resulted in a mixture of cyclopentanone products, with only 5% contamination by cycloheptenone **32** (Table II, entry 4).

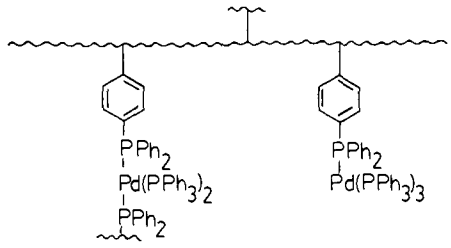


Figure 1. Polymer-bound Pd catalyst.

(33) Chow, Y. L.; Streith, J.; Taurand, G. *Org. Magn. Reson.* **1973**, *5*, 155. Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: Oxford, 1969; p 316.

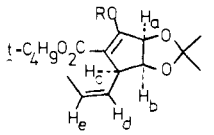
(34) Performed by K. J. Haller, University of Wisconsin—Madison, to whom we express our thanks.

(35) Extrapolated from the data of: Bordwell, F. G.; Van Der Puy, M.; Vanier, N. R. *J. Org. Chem.* **1976**, *41*, 1883.

(36) Cf.: Trost, B. M.; Keinan, E. *J. Am. Chem. Soc.* **1978**, *100*, 7779. Pittman, C. U. Jr.; Smith, L. R.; *Ibid.* **1975**, *97*, 341. Catalyst prepared by S. Springer in these laboratories, utilizing phosphinylated polystyrene prepared by the method of Card, R. J.; Neckers, D. C. *J. Org. Chem.* **1978**, *43*, 2958. Schwartz, R. H.; *Ibid.* **1979**, *44*, 2705.

The major cyclopentanone product **31** apparently arises by decarboalkoxylation of **30** caused by trace amounts of protic impurity. This process also occurred in $PhCH_3$ at reflux and resulted in a nearly identical mixture of products. The problem was easily solved by adding 2–4 equiv of *O,N*-bis(trimethylsilyl)acetamide to the reaction mixture before heating. The resulting proton-free environment allows the formation of 98% of the enol silyl ether (**35**) of the desired cyclopentanone **30**, contaminated by a trace (2%) of the cycloheptenone **32** (Table II, entry 5). This mixture can then be heated in wet Me_2SO to effect clean decarboalkoxylation and provide **31** in 82% isolated yield (Table II, entry 6).

Compounds **30–32** were isolated pure and fully characterized. Cyclopentanone **30** existed as a 64:36 ratio of keto to enol forms (enol form **34**), each one of which was easily resolved in the



34 R=H
35 R=TMS

270-MHz ^1H NMR spectrum. The absorptions assigned to **30** are δ 1.35 (s, 3 H), 1.45 (br s, 12 H), 1.72 (dd, 3 H, J = 6.7, 1.7 Hz), 3.36 (d, 1 H, J = 12.1 Hz, H_f), 3.56 (dddd, 1 H, J = 12.1, 9.5, 4.0, 0.7 Hz, H_c), 4.32 (d, 1 H, J = 5.0 Hz, H_a), 4.70 (dd, 1 H, J = 5.0, 4.0 Hz, H_b), 5.53 (ddq, 1 H, J = 10.5, 9.5, 1.7 Hz, H_d), 5.76 (dqd, 1 H, J = 10.5, 6.7, 0.7 Hz, H_e). The 10.5-Hz value for J_{de} and the ^{13}C shift of δ 13.4 for the vinyl methyl carbon confirm the presence of the (*Z*)-1-propenyl group. The large J_{bc} (4.0 Hz) confirms that the acetonide is cis to the 1-propenyl substituent, and the large J_{cf} (12.1 Hz) shows that these protons are trans to one another, as is expected.

The remainder of the spectrum corresponds to enol **34**: δ 1.35 (s, 3 H), 1.45 (br s, 12 H), 1.72 (dd, 3 H, J = 6.7, 1.7 Hz), 3.79 (ddd, 1 H, J = 10.2, 6.1, 0.6 Hz, H_c), 4.67 (t, 1 H, J = 6.1 Hz, H_b), 4.95 (d, 1 H, J = 6.1 Hz, H_a), 5.35 (ddq, 1 H, J = 10.9, 10.2, 1.7 Hz, H_d), 5.63 (dqd, 1 H, J = 10.9, 6.7, 0.6 Hz, H_e). The values for J_{de} (10.9 Hz) and the ^{13}C vinyl methyl shift (δ 13.3) corroborate the (*Z*)-1-propenyl group which is cis to the acetonide due to the large value for J_{bc} (6.1 Hz). The enol form is evident in the ^{13}C NMR chemical shift of the olefinic carbon bearing the ester group (δ 104.4) and in the IR band at 1660 cm^{-1}. The hydroxyl band is seen at 3250 cm^{-1} and the ester carbonyl at 1720 cm^{-1}. Chemical correlation of the tautomeric nature of these two compounds, **30** and **34**, was achieved by decarboalkoxylation of the mixture (by heating in moist Me_2SO) to provide a single compound, **31**.

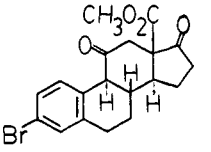
The 270-MHz ^1H NMR of the crude compound **35** was sufficiently clean to verify its structure. Irradiation at δ 3.81 (H_c) caused the following perturbations: (1) the collapse of H_d (ddq, J = 11.0, 10.5, 1.8 Hz) to a d of q (J = 11.0, 1.8 Hz), (2) the collapse of H_e (dqd, J = 11.0, 7.0, 0.8 Hz) to a d (J = 6.1 Hz). The value of J_{de} (11.0 Hz) confirms the (*Z*)-1-propenyl group, which is cis to the acetonide due to the large value for J_{bc} (6.1 Hz). The IR spectrum now shows only the olefin band of the enol at 1630 cm^{-1} and the ester carbonyl group at 1705 cm^{-1}.

The decarboalkoxylated cyclopentanone derivative **31** exhibits a single carbonyl band at 1755 cm^{-1} in its IR spectrum. The *Z* nature of the olefin is shown by J_{de} = 10.6 Hz and the ^{13}C shift of the vinyl methyl carbon (δ 13.2). The two protons H_f represent the AB portion of an ABX pattern, X = H_c. Irradiation of H_c (δ 3.13) effects the following transformations: (1) the collapse of H_d (ddq, J = 11.0, 10.6, 1.4 Hz) to a d of q (J = 10.6, 1.4 Hz), (2) the collapse of H_e (dqd, J = 10.6, 6.5, 0.8 Hz) to a d of q (J = 10.6, 6.5 Hz), (3) the collapse of H_f (m) to δ 2.27 (d, J = 18.4 Hz) and 2.37 (d, J = 18.4 Hz), and (4) the collapse of H_b (t, J = 4.3 Hz) to a d (J = 4.3 Hz). This substantial value for J_{bc} (4.3 Hz) demonstrates the retention of the cis relationship of the 1-propenyl group and the acetonide.

Cycloheptenone **32** distinguished itself by its 1740- and 1715-cm^{-1} IR bands for both the ester and ketone carbonyl groups. The *Z* nature of the olefin is shown by the 10.8-Hz coupling constant between H_d and H_e. Irradiation at δ 3.07 (H_c) effects the following perturbations: (1) the collapse of the allylic methyl group protons δ 1.14 (d, J = 6.1 Hz) to a singlet, (2) the collapse of H_d (ddd, J = 10.8, 6.0, 2.2 Hz) to a d of d (J = 10.8, 2.2 Hz), (3) the collapse of H_e (dt, J = 10.8, 1.9 Hz) to a d of d (J = 10.8, 1.9 Hz), (4) the collapse of H_f (d, J = 12.1 Hz) to a singlet, and (5) the collapse of H_b (ddt, J = 8.3, 2.2, 1.8 Hz) to a d of d of d (J = 8.3, 2.2, 1.9 Hz).

As was discussed for cycloheptenone **27**, the extraordinary homoallylic coupling of H_b and H_c (1.7 Hz) requires the allylic methyl group to be cis to the acetonide. The downfield shift of H_c (δ 3.07) indicates that it is deshielded by a cis relationship to the ester group. Furthermore, the large value of J_{cf} (12.1 Hz) assures the trans orientation of H_c and H_f. The allylic methyl carbon is found at δ 18.3. The ^1H and ^{13}C NMR spectra bear great resemblance to those of the amide analogue **27**, whose structure was verified by X-ray analysis (vide supra).

The potential of this methodology in steroid synthesis led us to consider the highly functionalized **36** as a target. The benefit



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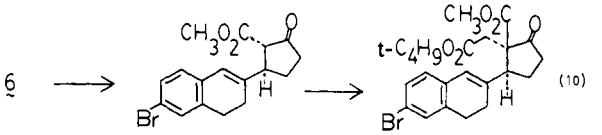
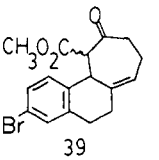
of the 11-oxo substituent is well-known from research into contraceptive agents (11β-methyl)[37] and the corticoid antiinflammatory agents (11β-hydroxy).[38] Less well-known is the necessity for higher oxidation levels at C-18 in the glucocorticoids and the antidiuretic aldosterone.[38] The bromine substituent at C-3 provides the chemical handle to attach a wide variety of different atoms and groups in the constant search for more potent drugs with fewer undesirable side effects. Many plants contain steroid alkaloids possessing a trialkylamine at C-3.[39]

Rearrangement of **6** proceeded smoothly upon subjection to 5% $(dppe)_2Pd$ in Me_2SO at 65 °C for 1.5 h to give an 81% yield of the desired cyclopentanone **37** as a 93:7 ratio of the *E* and *Z*



37 **38**

isomers. By combining all of the impurity bands from the TLC purifications of several large-scale reactions of enol ether **6**, it was possible to isolate a very small portion (<5%) of the other possible regioisomer, the cycloheptenone **39** as a 33:67 stereoisomeric



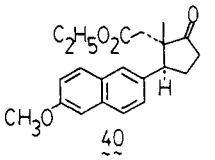
39

mixture. This product showed IR bands at 1740 and 1714 cm^{-1}; the cyclopentanone **37** possessed these bands at 1765 and 1725 cm^{-1}. The most definitive difference was in the UV spectra of the two compounds, **37** (5.4×10^{-5} M in MeOH), 271 (ϵ 17 040), 279 (17 960), and 291 (11 110) nm, and **39** (9.4×10^{-4} M in MeOH), 258 (ϵ =1600), 263 (1700), and 270 (1600) nm. The hypsochromic shift of **39** is further evidence for the cycloheptenone

(37) Baran, J. S. U.S. Patents 3,325,520, 3,377,366, 1967.
(38) Lednicer, D.; Mitscher, L. A. "The Organic Chemistry of Drug Synthesis", Wiley-Interscience: New York, 1977.
(39) Akhrem, A.; Titov, Y. "Total Steroid Synthesis", Plenum Press: New York, 1972.

structure which lacks the styrene chromophore.

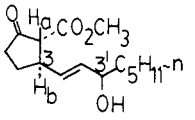
To finish the synthesis of the secosteroid analogue, we alkylated the cyclopentanone **37** by *tert*-butyl iodoacetate with K_2CO_3 in acetone to give 86% of the C-alkylation product **38** as a single stereoisomer (as indicated by 50.1-MHz ^{13}C NMR). A similar intermediate, **40**, has been recently converted to (±)-11-



40

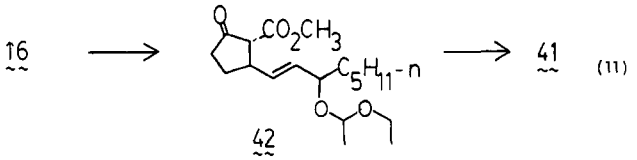
oxoequilenin methyl ether[40] by a simple four-step procedure in 52% overall yield. A similar set of reactions on **38** should yield the highly flexible steroidal analogue, **36**.

The cyclopentanone **41** constituted a second target since alkylation and decarbomethoxylation transform it to 11-deoxy-PGE, a source of several biologically active prostaglandin analogues.[41-43]



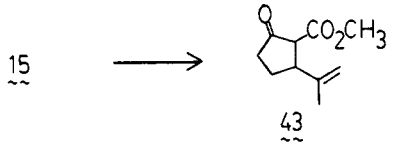
41

The $(dppe)_2Pd$ catalyst (7 mol % Me_2SO, 100 °C, 3 h) smoothly induces the rearrangement of the tetrahydrofuran **16** in the presence of *O,N*-bis(trimethylsilyl)acetamide for prevention of decarbomethoxylation (eq 11). Removal of the ethoxyethyl



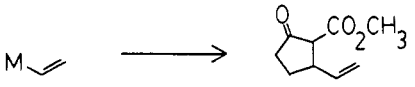
(11)

protecting group with acetic acid in aqueous THF to generate **41** simplifies the characterization. Use of benzene-d_6 as solvent in the 270-MHz ^1H NMR spectrum resolves the signals for the olefinic protons and for H_b (see formula **41**) for the two diastereomers. An olefinic coupling constant of $J = 16.2$ Hz confirms the pure *E* geometry. The trans ring stereochemistry is suggested by $J_{ab} = 12$ Hz. An approximately equal ratio of diastereomers is indicated by two signals for H_b at 2.77 and 2.79. The ^{13}C NMR spectrum further supports that interpretation by a doubling of peaks for C(3) (δ 43.6 and 43.7, two d) and C(3′) (δ 72.3, 72.4, two d). The isomeric nature of the mixture was proven by obtention of a satisfactory combustion analysis. For completeness, alkylidenetetrahydrofuran **15** was also rearranged to its cyclopentanone **43** (eq 12) under our standard conditions. These two



(12)

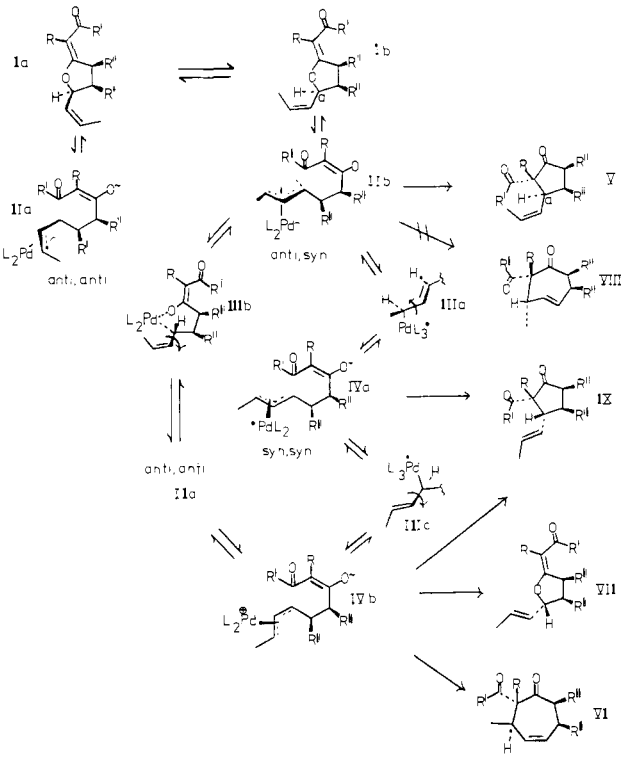
examples, which proceed in 34–43% overall yield, demonstrate the efficiency of converting a vinylorganometallic to the versatile 3-vinyl-2-carbomethoxycyclopentanones (eq 13).



(13)

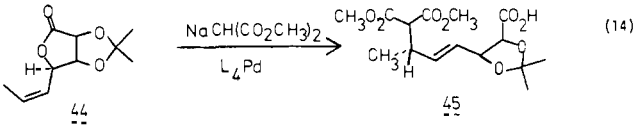
(40) Posner, G.; Chapdelaine, M.; Lentz, C. *J. Org. Chem.* **1979**, *44*, 3661.
(41) Kondo, K.; Umemoto, T.; Takahatake, Y.; Tunemoto, D. *Tetrahedron Lett.* **1977**, 113.
(42) Taber, D. F. *J. Am. Chem. Soc.* **1977**, *99*, 3513.
(43) Tow, T.; Kurozumi, S.; Tanaka, T.; Miura, S. *Tetrahedron Lett.* **1976**, 4087.

Scheme III. Rearrangement Pathway of 2-Alkylidene-5-vinyltetrahydrofuran



Discussion

In addition to the synthetic aspects, the experiments provide a much better understanding of the rearrangement and the nature of palladium-catalyzed alkylations. Firstly, the stereochemical specificity is extraordinarily high, as shown by the rearrangement of the carbohydrate substrates **20** and **21**. In considering the consequences of these results with respect to the allylic carbon bearing oxygen, C(5), we should anticipate that the initial ionization occurs with inversion of configuration.[30] All of the intermolecular alkylations appear to involve such a stereochemical result. Most pertinent to the present results is the rearrangement of **44**, which produced a single product **45** (eq 14), which results



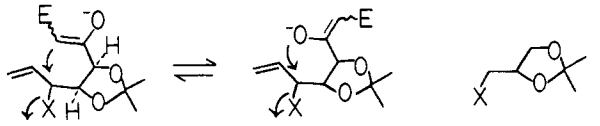
(14)

from ionization from a single conformer of **44** and the ionization and substitution steps each proceeding with inversion of configuration.[44] In the present case, assuming that the initial ionization occurs with inversion as for the typical bimolecular displacements, an overall picture emerges as summarized in Scheme III. Ionization from Ia is disfavored due to the unfavorable eclipsing interactions associated with forming the anti–anti complex IIa. The anti–syn complex IIb, which arises by ionization from conformer Ib, can either undergo syn–anti interconversions via σ complex IIIa or IIIb or ring closure at O or C to form five-membered rings, the tetrahydrofurans I or cyclopentanones V, respectively. Any seven-membered ring products arising from IIb would necessarily contain a trans double bond (e.g., VIII) and therefore is rather unlikely. Syn–anti interconversion to IVb is required for formation of seven-membered-ring products. Thus, the high selectivity in virtually all the rearrangements for cyclopentanone formation arises from a more rapid C-alkylation for IIb compared to the syn–anti interconversions of the π-allyl unit.

The carbohydrates **20** and **21** represent the exception; i.e., syn–anti interconversion not only competes but can dominate. This

(44) Trost, B. M.; Klun, T. P. *J. Am. Chem. Soc.* **1979**, *101*, 6756.

change in reactivity can be understood by considering the ring-closure step as a simple displacement in which the leaving group happens to be palladium, such as in **46**, X = PdL_2. The presence



46a 46b 47

of the adjacent acetonide generally decreases the rate of S_N2 displacements in systems like **47**. By slowing the alkylation, the syn–anti interconversion now successfully competes. The two possible isomerizations involve the σ-complexes IIIa and IIIb. While isomerization via IIIa produces the thermodynamically most stable π-allyl complex, the syn,syn isomer IVa, no cycloalkanones arise from this isomer. As in the case of the anti,syn complex IIb, geometrical considerations preclude the formation of seven-membered ring products, i.e., formation of VIII, and the presence of the acetonide hampers cyclopentanone formation. On the other hand, O-alkylation produces VII, a type of product that has been isolated from **21**, i.e., **33**. The steric and electronic demands of an oxygen nucleophile such as in **46b** would be expected to be much less stringent than that of a carbon nucleophile as in **46a**. Thus, while C-alkylation for formation of the cyclopentanone does not compete with syn–anti interconversion, five-membered-ring formation via O-alkylation does. Such O-alkylation from IIb regenerated starting material, and it is thus an invisible reaction.

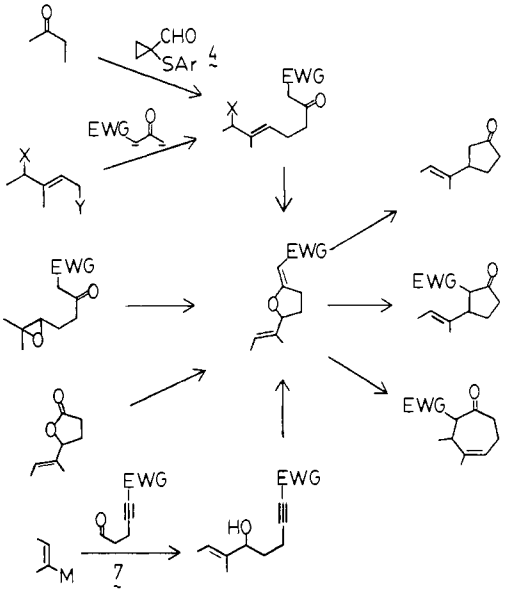
This same O-alkylation product can arise from the syn,anti complex IVb which would be the product of a further syn–anti interconversion from IVa via IIIc. Alternatively, IVb can arise via two syn–anti interconversions that proceed via IIIb to the anti,anti complex. Since syn–anti interconversion is facilitated by additional ligation, the possibility of internal coordination as in IIIb may favor such a pathway over the alternative. Internal alkylation to form the cyclopentanone IX from IVb suffers from the problems mentioned above, whereas alkylation at the more distal carbon of the π-allyl unit to form cycloheptenone minimizes the effect of the acetonide. Indeed, in the case of IVb, C-alkylation proceeds exclusively to form VI in the carbohydrate series.

For cyclopentanone formation, syn–anti interconversion must be disfavored relative to C-alkylation. Sterically small ligands facilitate formation of σ-palladium species. Thus, syn–anti interconversion should decrease in the order dppe > Ph_3P > (PS)-Pd as observed. Furthermore, the known ability of Me_2SO to serve as an additional ligand to palladium which results in increased rates of syn–anti interconversion[45] should and experimentally does increase seven-membered-ring product at the expense of five-membered. Thus, for the carbohydrate **21**, use of the smallest ligand in Me_2SO (maximum rate for syn–anti interconversion) gives only cycloheptenone, but use of the largest ligand in toluene (minimum rate for syn–anti interconversion) gives only cyclopentanone. In cases that do not possess the perturbing acetonide group, C-alkylation normally dominates syn–anti interconversion, and five-membered ring formation is the expected and observed course.

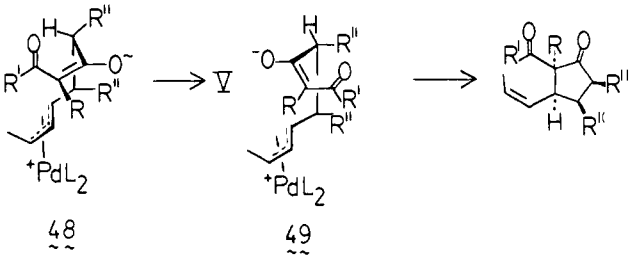
The stereochemical control is complete. As implied in the sequence Ib → IIb → V (Scheme III), an overall retention of stereochemistry at C(a) with *no* allyl inversion is observed. Since related results support the hypothesis that the initial ionization proceeds with inversion of configuration, the C–C bond-forming step also must occur with inversion. A similar explanation applies to the stereochemical course for cycloheptenone formation except that overall retention of stereochemistry with allyl inversion is observed. The remarkable formation of a single stereoisomer at the carbon α to the carbonyl groups in **26** and **27** can be understood considering nonbonded interactions in the transition states as discussed previously.[14] For example, comparison of **48** and **49**

(45) Faller, J. W. *Adv. Organomet. Chem.* **1977**, *16*, 211. Tsutsui, M.; Courtney, A. *Ibid.* **1977**, *16*, 241.

Scheme IV. Summary of Overall Synthetic Transformations



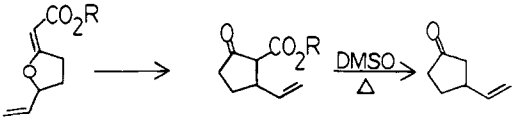
reveals a substantial nonbonded interaction between the carbonyl group and the acetonide (R″) in the latter. Thus, only the product derived from **48** forms.



48 49

The rearrangement of **6** further verifies the greater rate of the oxidative addition to the allyl system compared to the aryl bromide.[46] Since the aryl bromide must insert with retention of configuration whereas the allyl system proceeds with inversion, inversion mechanisms for palladium(0) appear to be of lower energy than retention mechanisms.

In the course of the rearrangements, we discovered a very mild procedure to effect a decarboalkoxylation of *tert*-butyl esters (eq 15, R = $CO_2C_4H_9$-*t*). Such decarboalkoxylations of methyl esters



(15)

have generally been discussed in terms of nucleophilic dealkylation of the ester followed by loss of carbon dioxide.[47] Such a mechanism is unlikely operable for a *tert*-butyl ester. It is more reasonable to assume that hydroxylic impurities facilitate an ionization of the *tert*-butyl carbenium ion which subsequently loses carbon dioxide. The role of such impurities is inferred from the ability of *O,N*-bis(trimethylsilyl)acetamide to preclude the decarboalkoxylation. The mildness of the reaction conditions is demonstrated by the decomposition of **30** when the reaction is attempted any other way. It is interesting to note that even in the case of methyl esters (eq 15, R = CH_3) decarbomethoxylation accompanies rearrangement in both dioxane and Me_2SO.[15,17] Once again, addition of *O,N*-bis(trimethylsilyl)acetamide eliminates this reaction.

(46) Kochi, J. K. "Organometallic Mechanisms and Catalysis"; Academic Press: New York, 1978.

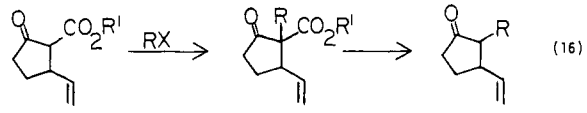
(47) For a leading reference, see: Krapcho, A. P.; Weimaster, J. F.; Eldridge, J. M.; Jahngen, E. G. E., Jr.; Lovey, A. J.; Stephens, W. P. *J. Org. Chem.* **1978**, *43*, 138.

Conclusions

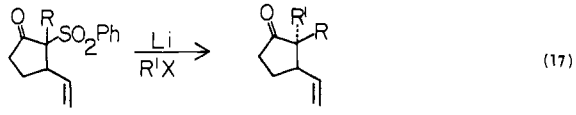
Four general routes to the preparation of 2-alkylidene-5-vinyltetrahydrofurans with any of several electron-withdrawing groups [EWG = CO_2R, SO_2Ph, $CON(C_2H_5)_2$] have been developed and are summarized in Scheme IV. Most noteworthy is the development of the two conjunctive reagents **4** and **7** as synthetic precursors. Conjunctive reagent **4** makes ketones, among the most accessible compounds, excellent building blocks. The wide variety of vinylorganometallic conjunctive reagents available in stereodefined form, especially from acetylenes, makes conjunctive reagent **7** especially valuable. Each of these has been demonstrated by the synthesis of a steroid and a prostaglandin precursor, respectively.

Two methods for the olefination of 4-vinyl-γ-butyrolactones have been developed. The availability of such substrates from carbohydrates suggests the applicability of this method in the synthesis of enantiomerically pure products.

2-Alkylidene-5-vinyltetrahydrofurans smoothly rearrange in excellent yield and with excellent stereocontrol to cyclopentanones in every case. In the case of EWG = CO_2CH_3 or $CO_2C_4H_9$-*t*, either the simple rearrangement product bearing the carboalkoxy group or the cyclopentanone which has undergone decarboalkoxylation may be isolated depending upon the reaction conditions. The presence of the EWG allows further regiocontrolled elaboration. When EWG = CO_2R, alkylation followed by decarboalkoxylation then constitutes an efficient approach to 2,3-disubstituted cyclopentanones (eq 16). When EWG = $PhSO_2$,



(16)



(17)

regiocontrolled enolate generation and alkylation provide a stereocontrolled synthesis of 2,2,3-trisubstituted cyclopentanones.

This cyclopentanone synthesis represents the equivalent of a palladium-catalyzed 1,3-rearrangement; the availability of cycloheptenones in some cases represents the equivalent of a palladium-catalyzed 3,3-rearrangement (Claisen rearrangement). The inaccessibility of such rearrangements thermally in sterically hindered systems suggests more extensive applicability for this palladium-mediated version. A seemingly related [3.3] rearrangement of 1,5-dienes apparently proceeds via a much different mechanism considering Pd(2+) catalyzes that reaction, whereas Pd(0) catalyzes the one reported herein.[48] A most important aspect is the degree of control over reaction pathways offered by the use of transition-metal templates. By understanding of the delicate interplay of ligand effects in reactivity of such complexes, simple and rational variation of reaction conditions permits the same substrate to traverse quite disparate reaction pathways. In that fact lies both the strength and the challenge of transition-metal-mediated synthetic reactions.

Experimental Section

General. All reactions were run under a positive pressure of dry nitrogen unless otherwise noted. Anhydrous reactions were performed in flame-dried glassware which was cooled under nitrogen. Anhydrous solvents were transferred by oven-dried syringe. Solvents were distilled before use: hexamethylphosphoric triamide (HMPA), dimethyl sulfoxide (Me_2SO), dimethylformamide (DMF), acetonitrile (CH_3CN), dichloromethane (CH_2Cl_2), chloroform ($CHCl_3$), carbon tetrachloride (CCl_4), pyridine (pyr), benzene (C_6H_6), hexane (C_6H_{14}), and pentane (C_5H_{12}) from calcium hydride; diethyl ether (Et_2O), tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), 1,4-dioxane, and toluene ($PhCH_3$) from sodium benzophenone ketyl; *N*-methylpyrrolidinone (NMP) from barium oxide; thionyl chloride ($SOCl_2$) from triphenyl phosphite; acetone from K_2CO_3; methanol (MeOH) from magnesium. Solvents for use in $(dppe)_2Pd$-catalyzed reactions were deoxygenated by flushing with argon for 20–30 min. All palladium(0) catalysts were transferred under nitrogen atmosphere. Other reagents were used as obtained commercially. The term "in vacuo" refers to the removal of solvent on a Buchi–Brinkman Rotoevaporator at water-aspirator pressure followed by evacuation of the flask (~0.1 mm) for 15–30 min, except as noted otherwise for volatile compounds. Silica gel (Macherey–Nagel PNV_{254}) was used for analytical and all preparative (1.5 mm thick) thin-layer chromatography (TLC) and activated before use by heating at 120 °C for 2 h. Precoated, high-resolution analytical plates (Macherey–Nagel Nano-Plates SIL-$2OUV_{254}$) were also employed. Typical loadings on preparative plates were up to 80 mg on 20 × 10 cm; 80–200 mg on 20 × 20 cm; 200–450 mg on 20 × 40 cm. Column chromatography was accomplished with Grace (grade 62, 60–200 mesh) silica gel and Fisher (600–100 mesh) Florisil adsorbent. Removal of the material from silica gel was accomplished by successive washings with ethyl acetate (EtOAc). High-pressure liquid chromatography (HPLC) was performed analytically (up to 2 mg) on a Waters M6000 instrument with a μ-Porasil silica gel column (10 μm, Waters p/n27477) or preparatively on a Waters Prep500 instrument with a self-packed, semiprep (2.5 × 30 cm, μ-Porasil, 37–75 μm, 2–500 mg) silica gel column and a PrepPak-500 silica gel column (75 μm, 1–10 g). Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected. Boiling points are uncorrected. Gas chromatography was performed on a Varian Aerograph, Model 90P.

Proton (^1H) NMR spectra were determined in the indicated solvent on a Jeolco MH-100 (100 MHz) instrument unless otherwise noted that a Bruker WH-270 (270 MHz) spectrometer was used. Chemical shifts are reported in δ units, parts per million (ppm) downfield from tetramethylsilane (Me_4Si). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; b or br, broad. Coupling constants are reported in hertz (Hz). Infrared spectra (IR) were determined in the indicated solvent in 1-mm-thick solution cells on a Perkin-Elmer 267 or a Beckman AccuLab 7 instrument and are reported in cm^{-1}. Carbon (^{13}C) NMR spectra were determined on a Jeolco FX-60 (15.4 MHz) or a Jeolco FX-200 (50.1 MHz) spectrometer. Chemical shifts are reported in δ units, and splitting patterns are designated as with ^1H NMR. Mass spectra (MS) were obtained on an AEI-902 instrument at an ionizing current of 90 mA and an ionizing voltage of 70 eV unless otherwise noted. Data are reported as *m/e* (%). Microanalyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI. Optical rotations were determined on a Perkin-Elmer 141 instrument on precise solutions in the indicated solvent and concentration (c) and are reported in degrees.

Preparation of 5,5-(Ethylenedioxy)-1-(trimethylsilyl)pent-1-yne. To a stirred solution of distilled (trimethylsilyl)acetylene[49] (511.4 mg, 5.22 mmol) in 6.0 mL of dry THF at −78 °C was added a solution of *n*-butyllithium in hexane (1.5 M, 3.30 mL, 4.95 mmol). The mixture was allowed to warm to 0 °C over 0.5 h and stirred an additional 0.5 h. Dry HMPA (927 mg, 5.18 mmol) was added, followed by bromide **8**[19] (719.0 mg, 3.97 mmol), and the mixture was stirred at 0 °C for 8 h. After acidification to pH 4.5 with 5% aqueous NaH_2PO_4 solution (20 mL) and extraction with ether (3 × 20 mL), the combined organic layers were washed with H_2O (5 × 1 mL) and with brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo to yield crude product (766.6 mg, 97%).

Preparative TLC purification of another sample, using two elutions with 20% ethyl acetate in hexane (v/v), yielded pure product (R_f 0.5) as determined by analytical TLC and NMR: NMR (CCl_4) 0.05 (s, 9 H), 1.6–1.9 (m, 2 H), 2.26 (t, 2 H, *J* = 7 Hz), 3.6–4.0 (m, 4 H), 4.82 (t, 1 H, *J* = 5 Hz); IR (CCl_4) 2180, 1720 (w), 1440, 1410, 1365, 1330 cm^{-1}; MS (40 eV) 198 (0.2), 155 (0.5), 139 (4), 125 (4), 111 (4), 109 (7), 83 (7), 73 (100), 67 (6), 59 (8), 45 (34), 43 (14), 41 (6), 39 (5) (calcd for $C_{10}H_{18}O_2S$, 198.1076; found, 198.1086).

Preparation of 5,5-(Ethylenedioxy)pent-1-yne. To a stirred solution of 633.9 mg (3.2 mmol) of crude 5,5-(ethylenedioxy)-1-(trimethylsilyl)pent-1-yne in 9.0 mL dry MeOH at 25 °C were added wet KOH pellets (183.4 mg, 3.3 mmol). The mixture was stirred for 2 h, acidified with 5% aqueous NaH_2PO_4 solution (20 mL), and extracted with pentane (4 × 20 mL). The combined organic layers were washed with H_2O (3 × 2 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo to yield crude product (383.0 mg, 94%).

A smaller scale experiment, using pure starting silane, gave crude product which was Kugelrohr distilled [50–70 °C (11 mm)] to yield pure product (85%) as a clear, colorless oil: NMR (CCl_4) 1.6–1.9 (m, 2 H), 2.05–2.35 (m, 2 H), 3.6–3.9 (m, 4 H), 4.8 (t, 1 H, *J* = 5 Hz); IR (CCl_4) 3300, 2120, 1440, 1410, 1390, 1360 cm^{-1}; MS 126 (1), 125 (11), 106 (1),

(48) Overman, L. E.; Knoll, F. M. *J. Am. Chem. Soc.* **1980**, *102*, 865. Heimbach, P.; Malin, M. *J. Organomet. Chem.* **1973**, *49*, 483, 477.

(49) Kraihanzel, C. S.; Losee, M. L. *J. Organomet. Chem.* **1967**, *10*, 427.

105 (3), 99 (8), 92 (56), 91 (66), 86 (24), 81 (16), 77 (100), 75 (21), 74 (19), 73 (100), 71 (12), 69 (11), 67 (23), 65 (24), 63 (15), 58 (10), 57 (42), 56 (16), 55 (30), 54 (14), 53 (61), 52 (11), 51 (30), 50 (17), 45 (96), 44 (97), 43 (94), 42 (38), 41 (46), 40 (18), 39 (68), 38 (18) (calcd for $C_7H_{10}O_2$, 126.0681 found, 126.0679).

Preparation of Methyl 6,6-(Ethylenedioxy)hex-2-ynoate (9). To a stirred solution of 231 mg (~1.83 mmol) of crude 5,5-(ethylenedioxy)-1-pentyne in 4.2 mL of dry THF at −78 °C was added a solution of *n*-butyllithium in hexane (1.5 M, 1.50 mL, 2.25 mmol). After being stirred for 0.5 h the mixture was added slowly via cannula to a stirred solution of distilled methyl chloroformate (366.9 mg, 3.90 mmol) in 1.5 mL of dry THF at −78 °C, using 1.5 mL additional dry THF to ensure complete transfer. The mixture was allowed to warm to 25 °C over 1 h, acidified with 5% aqueous NaH_2PO_4 solution (10 mL), and extracted with ether (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo. Preparative TLC purification, using 40% ethyl acetate in hexane (v/v), yielded **9** (351.7 mg, R_f 0.4, 48% from bromide **8**) which was pure by analytical TLC and NMR.

Kugelrohr distillation [90–100 °C (0.8 mm)] of another sample yielded pure **8** (96% recovery) as a clear, colorless oil: NMR (CCl_4) 1.7–2.0 (m, 2 H), 2.4 (t, 2 H, J = 7 Hz), 3.6 (s, 3 H), 3.7–4.0 (m, 4 H), 4.8 (t, 1 H, J = 4 Hz); IR (CCl_4) 2240, 1720, 1435 cm^{-1}; MS 184 (0.0), 183 (0.4), 169 (0.2), 153 (0.7), 129 (0.3), 125 (0.7), 109 (3), 83 (3), 81 (4), 73 (100), 53 (8), 45 (37), 43 (7), 41 (5) (calcd for $C_9H_{12}O_4$, 184.0736; found, 184.0736). Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.50; H, 6.42.

Preparation of Methyl 6-Oxohex-2-ynoate (7). Method A. To a stirred solution of crude acetal **9** (817.3 mg, 4.44 mmol) in 5 mL of undistilled THF at 25 °C was added aqueous H_2SO_4 solution (0.5 N, 14 mL, 6 mmol). Sufficient additional THF (5 mL) was added to achieve a one-phase, homogeneous mixture which was stirred for 17 h at 25 °C, heated to reflux for 10 h, neutralized with saturated aqueous $NaHCO_3$ solution (10 mL), and extracted with ether (2 × 30 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo to give crude **7** (510.1 mg, 82%) which analytical TLC and NMR spectroscopy indicated contained ~10% starting acetal.

Method B. To a stirred solution of acetal **9** (2.0114 g, 10.93 mmol) in 10 mL of undistilled methanol at 25 °C under nitrogen was added aqueous sulfuric acid solution (0.5 N, 25 mL, 12.5 mmol). Sufficient undistilled THF (15 mL) was added to achieve a one-phase, homogeneous solution which was stirred at 25 °C for 2 h, heated to 60 °C for 5 h, cooled to 25 °C, neutralized with solid sodium bicarbonate, and extracted with ether (3 × 40 mL). The combined organic layers were washed with H_2O (2 × 1 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo (0.1 mm) to give crude **7** (1.1777 g, 77%) which analytical TLC and NMR spectroscopy indicated contained 10% starting acetal **9**. The crude oil was dissolved in 15 mL of undistilled THF, and aqueous H_2SO_4 solution (0.5 N, 12 mL, 6.0 mmol) was added. The homogeneous solution was stirred at 25 °C for 8 h. The reaction mixture was treated exactly as before to provide crude **7** (1.0612 g, 69%) which analytical TLC and NMR spectroscopy indicated contained less than 3% starting acetal **9**. Kugelrohr distillation [50–70 °C (0.01 mm)] yielded **7** (1.0016 g, 94% recovery, >97% pure) as a clear, colorless oil.

Preparative TLC purification of the crude material from a later experiment, using 50% ethyl acetate in hexane (v/v), yielded **7** (57%, R_f 0.5) which was pure by analytical TLC and NMR spectroscopy: NMR (CCl_4) 2.3–2.8 (m, 4 H), 3.63 (s, 3 H), 9.67 (s, 1 H). IR (CCl_4): 2240, 1715–1725, 1440 cm^{-1}; MS 140 (2), 125 (2), 117 (24), 116 (13), 111 (15), 109 (14), 95 (10), 85 (16), 81 (19), 80 (14), 79 (18), 73 (100), 59 (13), 55 (14), 53 (37), 45 (24), 44 (16), 43 (31), 41 (23), 39 (12) (calcd for $C_7H_8O_3$, 140.0474; found, 140.0474).

Preparation of (*E*)- and (*Z*)-Methyl 5-(Propen-2-yl)tetrahydrofuran-2-ylideneacetate (15). Method A. To a stirred solution of distilled aldehyde **7** (149.3 mg, 1.07 mmol) in 3.0 mL of dry THF at −109 °C under nitrogen was slowly added a 25 °C solution of 2-propenylmagnesium bromide (previously prepared from the bromide in THF, 0.5 M, 3.25 mL, 1.63 mmol) over 35 min. The resulting white slurry was stirred at −109 °C for 30 min, allowed to warm to −78 °C over 45 min, and then added slowly to a stirred, two-phase system of 5% aqueous NaH_2PO_4 solution (10 mL) and ether (10 mL) at 0 °C. The aqueous phase was separated and extracted with ether (2 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo to give crude methyl 6-hydroxy-7-methyloct-7-en-2-ynoate **10** (179.4 mg, 92%) as a clear, pale yellow oil which analytical TLC and NMR proved to be mostly the desired **10** with ~6% starting aldehyde **7**.

An earlier experiment utilized pure aldehyde **7** and furnished crude material which, after two separate preparative TLC purifications using two elutions with 40% acetone in hexane (v/v), yielded **10** (20% recovery, 12% yield, R_f 0.5) as a clear, pale yellow oil which NMR proved to be nearly pure: NMR (CCl_4) 1.74 (s, 3 H), 1.78 (t, 2 H, J = 7 Hz), 2.40 (t, 2 H, J = 7 Hz), 2.90 (s, 1 H), 3.75 (s, 3 H), 4.07 (t, 1 H, J = 7 Hz), 4.80 (broad s, 1 H), 4.95 (broad s, 1 H); IR (CCl_4) 3640, 3650–3200, 2250, 1710, 1440 cm^{-1}.

To a stirred solution of the crude allylic alcohol **10** (179.4 mg, theoretically 0.98 mmol) in 3.0 mL of distilled MeOH at 25 °C under nitrogen was added commercial 97% $PhSO_2Na$ (164.1 mg, 0.97 mmol) in one portion. The solution was stirred at 30 °C for 6 days (no change after 3 days) and partitioned between ether (20 mL) and saturated aqueous $NaHCO_3$ solution (20 mL). The aqueous phase was extracted with ether (2 × 20 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo to give crude **15** (177.0 mg, 99%). Preparative TLC purification, using two elutions with 40% acetone in hexane (v/v), yielded (*E*)-**15** (33.9 mg, 19% R_f 0.7) and (*Z*)-**15** (57.9 mg, 33%, R_f 0.5) as clear, pale yellow oils which were pure by analytical TLC and NMR. The *Z* isomer was unstable and isomerized to the *E* isomer on standing at 25 °C over several days. Kugelrohr distillation of (*E*)-**15** [92% recovery, 55–70 °C (0.03 mm)] gave a clear, colorless oil: NMR (270 MHz, $CDCl_3$) 1.89 (dq, 1 H, J = 12.5, 8 Hz), 2.23 (dm, 1 H, J = 12.5 Hz), 3.02 (dtd, 1 H, J = 18.5, 8.8, 1.6 Hz), 3.28 (dddd, 1 H, J = 18.5, 9.2, 5.0, 1.6 Hz), 3.66 (s, 3 H), 4.79 (t, 1 H, J = 7.5 Hz), 4.91 (bs, 1 H), 5.00 (bs, 1 H), 5.35 (t, 1 H, J = 1.6 Hz); IR (CCl_4) 1710, 1640, 1440, 1360, 1320 cm^{-1}; MS 183 (2), 182 (38), 167 (3), 151 (30), 150 (28), 135 (17), 127 (11), 123 (15), 122 (16), 109 (15), 101 (91), 95 (26), 94 (14), 83 (13), 82 (34), 81 (46), 80 (18), 79 (29), 77 (10), 69 (100), 69 (10), 67 (77), 59 (22), 55 (38), 53 (33), 43 (15), 41 (70), 40 (11), 39 (61) (calcd for $C_{10}H_{14}O_3$, 182.0943; found, 182.0947). The ethyl ester of (*E*)-**15** was purified by microdistillation [45 °C (0.01 mm)] for analysis. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.20; H, 8.10.

Spectra for (*Z*)-**15** were obtained as soon as possible following isolation: NMR (270 MHz, $CDCl_3$) 1.76 (s, 3 H) 1.87 (ddd, 1 H, J = 13.8, 8.4, 7.0 Hz), 2.19 (dq, 1 H, J = 13.8, 7.0 Hz), 2.74 (ddd, 2 H, J = 8.4, 7.0, 1.0 Hz), 3.68 (s, 3 H), 4.87 (t, 1 H, J = 1.0 Hz), 4.92 (d, 1 H, J = 0.8 Hz), 5.00 (t, 1 H, J = 7.0 Hz), 5.07 (d, 1 H, J = 0.8 Hz); IR ($CDCl_3$) 1705, 1655, 1440, 1370, 1300 cm^{-1}.

Method B. To a stirred solution of TLC-purified alcohol **10** (~90% pure, 59.6 mg, 0.30 mmol) in 1.0 mL dry MeOH at 25 °C under nitrogen was added commercial 97% $PhSO_2Na$ (54.0 mg, 0.32 mmol) in one portion. The solution was stirred for 46 h, and solvent was removed by evaporation with a stream of nitrogen. The residue was partitioned between ether (20 mL) and saturated aqueous $NaHCO_3$ solution (20 mL) and extracted with ether (2 × 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated in vacuo. Preparative TLC purification, using two elutions with 40% acetone in hexane (v/v), yielded (*E*)-**15** (14.8 mg, 27%, R_f 0.7), and (*Z*)-**15** (28.6 mg, 53%, R_f 0.5), which were pure by analytical TLC and NMR spectroscopy.

Preparation of Methyl 9-(1-Ethoxyethoxy)-6-hydroxytetradec-(*E*)-7-en-2-ynoate (11). To a stirred solution of distilled (*E*)-3-(1-ethoxyethoxy)-1-iodo-1-octene[50] (424.1 mg, 1.30 mmol) in 10.5 mL of dry ether at −78 °C under nitrogen was added a solution of *tert*-butyllithium in pentane (2.2 M, 1.23 mL, 2.71 mmol) dropwise. The clear, colorless solution was stirred at −78 °C for 2 h. A solution of $MgBr_2$ (1.86 M in 5% benzene/ether, 0.69 mL, 1.28 mmol) was added dropwise, and the resulting colorless slurry was stirred at −78 °C for 1 h. Distilled aldehyde **7** was added dropwise, and the thick, colorless slurry was stirred at −78 °C for 1 h and then allowed to warm to +5 °C over 1.5 h. The reaction mixture was added slowly to a stirred, two-phase system of 5% aqueous NaH_2PO_4 solution (10 mL) and ether (10 mL) at 0 °C. The aqueous phase was extracted with ether (2 × 20 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (10 mL), dried over Na_2SO_4, and concentrated in vacuo. TLC purification, using three elutions with 30% acetone in hexane (v/v), yielded pure **11** (172.4 mg, 58%) as determined by analytical TLC. ^1H NMR and ^{13}C NMR proved it to be a mixture of four diastereomers: ^1H NMR (270 MHz, $CDCl_3$) 0.88 (broad t, 3 H, J = 7.0 Hz), 1.176 (t, 0.75 H, J = 6.5 Hz), 1.178 (t, 0.75 H, J = 6.5 Hz), 1.196 (t, 1.5 H, J = 6.5 Hz), 1.286 (d, 1.5 H, J = 5.2 Hz), 1.296 (d, 1.5 H, J = 5.2 Hz), 1.3–1.6 (m, 8 H), 1.79 (q, 2 H, J = 6.0 Hz), 2.45 (broad s, 1 H), 2.47 (t, 2 H, J = 6.0 Hz), 3.4–3.7 (m, 2 H), 3.76 (s, 3 H), 3.906 (broad q, 0.25 H, J = 6.5 Hz), 3.916 (broad q, 0.25 H, J = 6.5 Hz), 4.03 (broad q, 0.50 H, J = 6.5 Hz), 4.27 (m, 1 H), 4.691 (quintet, 0.5 H, J = 5.2 Hz), 4.695 (quintet, 0.5 H, J = 5.2 Hz), 5.60 (m, 1 H), 5.68 (m, 1 H); IR ($CDCl_3$) 3620, 2600–3200, 2960, 2880, 2240, 1725, 1440, 1250, 1080, 860 cm^{-1}; ^{13}C NMR (50.1 MHz, $CDCl_3$) 154.0 (s), [134.3, 134.2, 133.2, 133.1, 133.0,

(50) Bernady, K. F.; Weiss, M. J. *Prostaglandins*, **1973**, *3*, 505. We thank Dr. Joseph Timko of the Upjohn Co. for a generous sample.

132.3 (d)], [99.2, 98.8, 97.6, 97.0 (d)], 89.1 (s), 88.4 (s), [77.3, 76.6, 76.4 (d)], [70.6, 70.4, 70.3 (d)], [60.8, 60.7, 50.1 (d)], 52.4 (q), [35.9, 35.6 (t)], 34.8 (t), 31.8 (t), [25.1, 24.8 (t)], 22.6 (t), [20.6, 20.4 (q)], [15.4, 15.3 (q)], 14.9 (t, 14.0 (q)).

Preparation of (*E*)- and (*Z*)-Methyl 5-[(*E*)-3-(1-Ethoxyethoxy)oct-1-en-1-yl]tetrahydrofuran-2-ylideneacetate (16). Method A. To a stirred solution of distilled aldehyde **7** (301.2 mg, 2.15 mmol) in 4.0 mL of dry ether and 2.0 mL of dry THF at −78 °C under nitrogen was slowly added a −78 °C slurry of (*E*)-3-(1-ethoxyethoxy)oct-1-en-1-ylmagnesium bromide (3.23 mmol, prepared as previously described) over 30 min. The flask that contained the Grignard reagent was rinsed with dry THF (2 × 1.5 mL), and these rinsings were cooled to −78 °C and added to the aldehyde solution. The resulting thick, colorless slurry was allowed to warm to −20 °C over 30 min and then cooled to −50 °C and stirred for 30 min. The reaction mixture was worked up as previously described to provide crude **11** (921.5 mg, 126%) as a clear yellow oil.

This crude material was further reacted in two separate experiments, the larger of which is described here.

To a stirred solution of crude **11** (641.1 mg, theoretically 1.89 mmol) in 5.2 mL of dry MeOH at 25 °C under nitrogen was added commercial 97% $PhSO_2Na$ (361.7 mg, 2.21 mmol) in two portions. The solution was stirred at 30 °C for 36 h and at 45 °C for 21 h. The solvent was removed by evaporation with a stream of nitrogen, and the residue was partitioned between ether (40 mL) and saturated aqueous $NaHCO_3$ (40 mL). The aqueous phase was extracted with ether (2 × 40 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (20 mL), dried over Na_2SO_4, and concentrated in vacuo. Preparative TLC purification, using four elutions with 30% acetone in hexane (v/v), yielded (*E*)-**16** (102.7 mg, R_f 0.9) and (*Z*)-**16** (230.1 mg, R_f 0.7) as yellow semisolids which were pure by analytical TLC and ^1H NMR and proven by ^{13}C NMR to be each a mixture of four diastereomers.

The smaller experiment provided 18.2 mg (*E*)-**16** and 40.0 mg (*Z*)-**16** making a total of (*E*)-**16** (120.9 mg, 17%) and (*Z*)-**16** (270.1 mg, 37%). The (*Z*)-**16** was unstable and isomerized to (*E*)-**16** upon heating. Kugelrohr distillaton of (*E*)-**16** [82% recovery, 160–180 °C (0.007 mm)] gave a clear, very pale yellow, semisolid: NMR (270 MHz, $CDCl_3$) 0.88 (broad t, 3 H, J = 6.5 Hz), 1.17 (t, 1.5 H, J = 6.5 Hz), 1.19 (t, 1.5 H, J = 6.5 Hz), 1.27 (d, 1.5 H, J = 5.2 Hz), 1.28 (d, 1.5 H, J = 5.2 Hz), 1.2–1.6 (m, 8 H), 1.83 (m, 1 H), 2.26 (m, 1 H), 3.00 (dtd, 1 H, J = 18.6, 9.3, 1.5 Hz), 3.27 (m, 1 H), 3.3–3.7 (m, 2 H), 3.66 (s, 3 H), 3.93 (quintet, 0.5 H, J = 6.0 Hz), 4.05 (quintet, 0.5 H, J = 6.0 Hz), 4.679 (q, 0.5 H, J = 5.2 Hz), 4.683 (q, 0.6 H, J = 5.2 Hz), 4.83 (q, 1 H, J = 6.5 Hz), 5.32 (dd, 1 H, J = 3.0, 1.5 Hz), 5.63 (m, 1 H), 5.70 (m, 1 H); IR ($CDCl_3$) 1705, 1640, 1435, 1360 cm^{-1}; MS 340 (0.1), 282 (0.3), 266 (0.8), 251 (5), 237 (2), 197 (5), 181 (1), 165 (1), 155 (1), 141 (3), 135 (4), 101 (2), 99 (2), 81 (1), 79 (1), 74 (2), 73 (100), 69 (1), 55 (1), 45 (32), 43 (3), 40 (2) (calcd for $C_{19}H_{32}O_5$, 340.2250; found, 340.2248); ^{13}C NMR (50.1 MHz, $CDCl_3$) 175.9 (s), 168.8 (s), [135.4, 135.3, 134.6, 134.5 (d)], [129.9, 129.7, 128.5, 128.4 (d)], [99.0, 97.2 (d)], [89.4, 89.3 (d)], [83.4, 83.3, 83.1 (d)], [76.0, 75.5 (d)], [60.9, 60.7, 59.3, 59.2 (d)], 50.5 (q), [35.7, 35.5 (t)], 31.7 (t), 30.2 (t), 30.1 (t), [25.0, 24.7 (t)], 22.5 (t), [20.6, 20.4 (q)], [15.4, 15.2 (q)], 14.0 (q).

Spectra for (*Z*)-**16** were obtained as soon as possible after isolation: NMR (270 MHz, $CDCl_3$) 0.88 (broad t, 3 H, J = 6.5 Hz), 1.18 (t, 1.5 H, J = 6.5 Hz), 1.19 (t, 1.5 H, J = 6.5 Hz), 1.28 (d, 1.5 H, J = 5.2 Hz), 1.29 (d, 1.5 H, J = 5.2 Hz), 1.2–1.6 (m, 8 H), 1.80 (m, 1 H), 2.20 (m, 1 H), 2.73 (t, 2 H, J = 6.5 Hz), 3.4–3.7 (m, 2 H), 3.67 (s, 3 H), 3.93 (q, 0.25 H, J = 6.1 Hz), 3.94 (q, 0.25 H, J = 6.1 Hz), 4.06 (q, 0.50 H, J = 6.1 Hz), 4.68 (q, 0.25 H, J = 5.2 Hz), 4.69 (q, 0.75 H, J = 5.2 Hz), 4.87 (quintet, 1 H, J = 1.2 Hz), 5.06 (qm, 1 H, J = 6 Hz), 5.68 (m, 1 H), 5.76 (m, 1 H); IR ($CDCl_3$) 1705, 1655, 1445, 1385, 1300 cm^{-1}; MS 340 (0.0), 251 (3), 237 (2), 219 (1), 197 (8), 165 (2), 155 (2), 141 (6), 135 (3), 121 (3), 109 (2), 107 (2), 101 (7), 99 (4), 95 (4), 91 (4), 81 (7), 79 (8), 73 (100), 69 (27), 67 (8), 55 (14), 45 (90), 44 (40), 43 (38), 41 (20), 40 (28). ^{13}C NMR (50.1 MHz, $CDCl_3$): 171.0 (s), 166.0 (s), [135.4, 135.0, 134.5 (d)], [129.6, 75.7, 75.6 (d)], [61.0, 60.8, 59.6, 59.2 (d)], 50.5 (q), [35.7, 35.5 (t)], [32.0, 31.9 (t)], 31.8 (t), 29.4 (t), [25.0, 24.8 (t)], 22.5 (t), [20.6, 20.4 (q)], [15.4, 15.3 (q)], 14.0 (q).

Method B. To a stirred solution of TLC-purified alcohol **11** (92.2 mg, 0.27 mmol) in 0.8 mL of distilled MeOH at 25 °C under nitrogen was added commercial 97% $PhSO_2Na$ (49.5 mg, 0.29 mmol) in one portion. The solution was stirred at 30 °C for 19 h and allowed to stand at 20 °C for 11 h. The majority of the solvent was evaporated by a stream of nitrogen, and the residue was purified by preparative TLC, using two elutions with 40% acetone in hexane (v/v), to yield (*E*)-**16** (34.0 mg, 37%, R_f 0.7) and (*Z*)-**16** (56.4 mg, 61%, R_f 0.8) as pale yellow semisolids.

Preparation of *N*,*N*-Diethyl-(*E*)-2-[2(*S*),3(*S*)-(isopropylidenedioxy)-5(*R*)-[(*Z*)-propenyl]tetrahydrofuran-2-ylidene]propionamide (20). To a stirred solution of lactone **19** (266.2 mg, 1.34 mmol) in 1.0 mL of dry THF at 10 °C under nitrogen was added solid, anhydrous $MgBr_2$ (314.3 mg, 1.71 mmol) in one portion. To the resulting slurry, distilled 1-(diethylamino)propyne (298.7 mg, 2.69 mmol) was added slowly. The orange slurry was stirred at 0 °C for 15 min, then allowed to warm to 25 °C, and stirred for 5 h. The reaction mixture was quenched with water (10 mL) and extracted with methylene chloride (2 × 15 mL). The combined organic layers were washed with brine (5 mL), dried (Na_2SO_4), and concentrated in vacuo to give 571 mg of dark red-brown oil. This oil was filtered through Florisil (8 × 1.5 cm) with 50% (v/v) ethyl acetate in hexane (120 mL) and concentrated in vacuo to give 415.9 mg of yellow, crystalline solid. Recrystallization from hot hexane gave pure **20** (284.2 mg, 68%) as colorless needles, mp 69.5–70.5 °C. TLC purification of the mother liquor, using 100% ethyl acetate, yielded additional **20** (78.4 mg, 19%, R_f 0.4) as a pale yellow solid: NMR (270 MHz, $CDCl_3$) 1.17 (t, 6 H, J = 7 Hz), 1.32 (s, 3 H), 1.44 (s, 3 H), 1.75 (dd, 3 H, J = 6.9, 1.7 Hz), 1.84 (d, 3 H, J = 0.6 Hz), 3.33 (m, 2 H), 3.50 (m, 2 H), 4.66 (dd, 1 H, J = 5.9, 4.1 Hz), 4.83 (ddd, 1 H, J = 8.3, 4.1, 0.8 Hz), 5.28 (dq, 1 H, J = 5.9, 0.6 Hz), 5.70 (ddq, 1 H, J = 11, 8.3, 1.7 Hz), 5.83 (dqd, 1 H, J = 11, 6.9, 0.8 Hz); IR ($CHCl_3$) 1690, 1605, 1460, 1440, 1380 cm^{-1}; MS 310 (3), 309 (24), 294 (4), 237 (31), 179 (21), 168 (8), 156 (19), 155 (10), 151 (29), 137 (8), 127 (13), 125 (23), 109 (12), 100 (17), 97 (13), 95 (13), 83 (100), 81 (10), 72 (41), 67 (16), 59 (12), 58 (32), 56 (16), 55 (23), 44 (34), 43 (92), 42 (12), 41 (20), 40 (26). ^{13}C NMR (50.1 MHz, $CDCl_3$): 170.4 (s), 152.7 (s), 130.2 (d), 124.1 (d), 112.4 (s), 107.9 (s), 80.0 (d), 78.5 (d), 77.8 (d), 43–38 (two t), 26.4 (q), 25.4 (q), 13.6 (q), 13.5 (q), 13.2–12.8 (two q); $[\alpha]^{25}_D$ +201.9° (c 2.58, CH_2Cl_2). Anal. Calcd for $C_{17}H_{27}O_4N$: C, 65.99; H, 8.80; N, 4.53. Found: C, 65.84; H, 8.64; N, 4.41.

Preparation of *tert*-Butyl (*E*)- and (*Z*)-[2(*S*),3(*S*)-(Isopropylidenedioxy)-5(*S*)-[(*Z*)-propenyl]tetrahydrofuran-2-ylidene]acetate (21). To a stirred solution of distilled diisopropylamine (121.3 mg, 1.20 mmol) in 1.5 mL of dry THF at −78 °C under nitrogen was added a solution of *n*-butyllithium (1.45 M in hexane, 0.83 mL, 1.20 mmol) dropwise. After this was stirred for 10 min, a solution of *tert*-butyl acetate (139.6 mg, 1.20 mmol) in 0.34 mL of dry THF was added over 10 min. This clear, very pale yellow solution was stirred at −78 °C for 1 h. The crystalline lactone **19** (199.8 mg, 1.01 mmol) was added in portions, and the mixture was stirred at −78 °C for 2 h to provide a cloudy, colorless solution which was quenched with 1.5 mL of ethanol, warmed to −20 °C, and poured into 5% aqueous NaH_2PO_4 (15 mL). The solution was extracted with ether (3 × 15 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo to 290.0 mg of pale yellow viscous oil.

This crude material was dissolved in 3.6 mL dry THF. To the stirred solution at 0 °C under nitrogen was added distilled DBU (458.1 mg, 3.01 mmol) and distilled methanesulfonyl chloride (312.3 mg, 2.74 mmol). An amorphous white solid formed, and the mixture was stirred at 0 °C for 1 h. Additional DBU (274.9 mg, 1.80 mmol) was added. The mixture was stirred at 0 °C for 3.5 h, quenched with 5% aqueous NaH_2PO_4 (15 mL), and extracted with ether (3 × 15 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo to give 279.9 mg of pale yellow oil. TLC purification, using two elutions with 50% ethyl acetate in hexane (v/v), yielded **21a** (176.5 mg, 59%, R_f 0.9) as a clear, colorless oil and **21b** (78.8 mg, 26%, R_f 0.8) as a colorless solid. **21a**: NMR (270 MHz, $CDCl_3$) 1.41 (s, 3 H), 1.44 (s, 3 H), 1.49 (s, 9 H), 1.76 (dd, 3 H, J = 7.0, 1.7 Hz), 4.72 (dd, 1 H, J = 6.0, 4.0 Hz), 4.92 (ddd, 1 H, J = 8.3, 4.0, 0.9 Hz), 5.34 (d, 1 H, J = 1.3 Hz), 5.68 (ddq, 1 H, J = 10.8, 8.3, 1.7 Hz), 5.71 (dd, 1 H, J = 6.0, 1.3 Hz); IR ($CDCl_3$) 1695, 1655, 1450, 1365, 1340, 1320 cm^{-1}; MS (30 eV) 296 (4), 240 (19), 225 (8), 223 (17), 220 (18), 219 (32), 218 (33), 182 (32), 165 (16), 164 (11), 158 (12), 141 (16), 140 (79), 112 (78), 100 (12), 96 (11), 95 (13), 91 (44), 84 (13), 83 (16), 82 (12), 81 (13), 80 (12), 71 (42), 69 (25), 67 (18), 59 (43), 57 (85), 56 (30), 55 (53), 45 (25), 44 (93), 43 (100), 41 (66), 40 (81), 36 (16); $[\alpha]^{25}_D$ +335.7° (c 1.92, CH_2Cl_2). Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.73; H, 8.19. **21b**: NMR (270 MHz, $CDCl_3$) 1.37 (s, 3 H), 1.46 (s, 9 H), 1.47 (s, 3 H), 1.75 (dd, 3 H, J = 6.7, 1.6 Hz), 4.65 (dd, 1 H, J = 5.4, 3.7 Hz), 5.03 (d, 1 H, J = 1.0 Hz), 5.12 (dd, 1 H, J = 5.4, 1.0 Hz), 5.25 (ddd, 1 H, J = 8.4, 3.7, 0.7 Hz), 5.74 (ddq, 1 H, J = 11.0, 8.4, 1.6 Hz), 5.88 (dqd, 1 H, J = 11.0, 6.7, 0.7 Hz); IR ($CHCl_3$) 1700, 1655, 1380, 1370, 1300 cm^{-1}; MS (32 eV) 296 (0.5), 2.81 (1.2), 240 (8), 225 (10), 223 (15), 182 (24), 165 (15), 158 (12), 140 (89), 125 (12), 112 (64), 100 (22), 97 (12), 95 (23), 84 (14), 83 (10), 81 (21), 71 (37), 69 (14), 67 (18), 59 (51), 57 (100), 56 (20), 55 (58), 44 (12), 43 (65), 41 (96), 39 (14). A small sample of **21b** was recrystallized from hexane to give colorless needles, mp 96–104 °C, with decomposition. Analytical TLC of the melted crystals showed substantial rearrangement to the more stable **21a**: $[\alpha]^{25}_D$ +226.9° (c 4.94, CH_2Cl_2). Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 64.71; H, 8.04.

Preparation of *N*,*N*-Diethyl-2(*S*)-carboxamido-4(*S*),5(*S*)-(iso-

propylidenedioxy)-2(*S*)-methyl-3(*S*)-[(*Z*)-propenyl]cyclopentanone (26). Method A (Table I, entry 3). To a stirred solution of enol ether **20** (40.1 mg, 0.13 mmol) in 0.7 mL of dry, deoxygenated dioxane at 25 °C under argon was added $Pd(dppe)_2$ (9.5 mg, 0.01 mmol). The yellow solution was heated rapidly to 90 °C, stirred for 1 h, cooled, and concentrated in vacuo. Proton NMR and analytical HPLC (20% ethyl acetate in hexane, 2.0 mL/min) analyses of the crude material revealed only one compound (t_R 4.3 column volumes). TLC purification, using two elutions with 50% ethyl acetate in hexane (v/v), yielded **26** (37.4 mg, 93%, R_f 0.5) which was pure by 270-MHz ^1H NMR and TLC: ^1H NMR (270 MHz, $CDCl_3$) 1.11 (t, 6 H, J = 7.0 Hz), 1.34 (s, 3 H), 1.39 (s, 3 H), 1.46 (s, 3 H), 1.68 (dd, 3 H, J = 7.0, 2.0 Hz), 3.17 (m, 2 H), 3.35 (m, 2 H), 3.73 (ddd, 1 H, J = 10.5, 4.9, 0.8 Hz), 4.73 (m, 2 H), 5.48 (ddq, 1 H, J = 11, 10.5, 2.0 Hz), 5.82 (dqd, 1 H, J = 11, 7.0, 0.8 Hz); IR ($CDCl_3$) 2960, 2960, 2900, 2860, 1755, 1745, 1620, 1600, 1460, 1430, 1380, 1275, 1260, 1220, 1155, 1100, 1080, 970 cm^{-1}; ^{13}C NMR (50.1, MHz, $CDCl_3$) 210.7 (s), 171.2 (s), 128.5 (d), 124.2 (d), 112.9 (s), 80.0 (d), 77.6 (d), 59.4 (s), 41.7 (d), 41.0 (t), 26.3 and 25.0 (q, acetonide methyls), 17.8 (q, angular CH_3), 13.3 (q, vinyl CH_3), 12.8 (q, amide methyls). Purification of a small portion by collection from analytical HPLC (15% ethyl acetate in hexane, 2.0 mL/min, (t_R 6.6 column volumes) provided **26** as a clear, colorless oil: MS 309 (24), 294 (2), 281 (0.5), 223 (1), 194 (7), 182 (14), 181 (6), 171 (6), 166 (3), 151 (32), 140 (2), 123 (3), 109 (22), 100 (100), 95 (5), 85 (9), 81 (6), 72 (20), 58 (11), 55 (9), 44 (19), 43 (26), 41 (16); $[\alpha]^{25}_D$ +22.0 (*c* 1.59, CH_2Cl_2). Anal. Calcd for $C_{17}H_{27}O_4N$: C, 65.99; H, 8.80; N, 4.53. Found: C, 65.76; H, 8.62; N, 4.48.

Method B (Table I, entry 1). To a stirred solution of **20** (149.5 mg, 0.48 mmol) in 2.2 mL of dry, deoxygenated Me_2SO at 25 °C under argon was added $(dppe)_2Pd$ (26.3 mg, 0.03 mmol). The solution was heated rapidly to 120 °C, stirred for 2 h, cooled, and concentrated in vacuo. TLC purification, using two elutions with 50% ethyl acetate in hexane (v/v), yielded pure **26** (52.0 mg, 35%, R_f 0.5), a mixture of two new cyclopentanones (26.1 mg, 17%, R_f 0.6), and pure *N,N*-diethyl-2(*S*)-carboxamido-6(*S*),7(*S*)-(isopropylidenedioxy)-3(*R*)-methyl-2(*S*)-methylcyclohept-4-enone (**27**, 40.7 mg, 27%, R_f 0.7) as a colorless solid: ^1H NMR (270 MHz, $CDCl_3$): 1.10 (t, 6 H, J = 7 Hz), 1.19 (d, 3 H, J = 6.8 Hz), 1.33 (s, 3 H), 1.38 (s, 3 H), 1.61 (s, 3 H), 3.16 (m, 2 H), 3.31 (m, 2 H), 3.54 (quintet of t, 1 H, J = 6.8, 1.4 Hz) [sequential irradiation at 1.19, 5.14, 5.38, and 5.74 shows 3.54 (quintet of dd, 1 H, J = 6.8, 1.5, 1.3 Hz)], 5.14 (m, 2 H), 5.38 (ddd, 1 H, J = 10.5, 6.8, 2.0 Hz), 5.74 (dt, 1 H, J = 10.5, 1.5 Hz); IR ($CDCl_3$) 1725, 1620, 1455, 1420, 1380 cm^{-1}; ^{13}C NMR (50.1 MHz, $CDCl_3$) 204 (s), 168.1 (s), 134.1 (d), 130.9 (d), 110.2 (s), 79.5 (d), 76.8 (d), 66.4 (s), 42.0 (two t), 36.6 (d), 26.4 and 25.0 (q, acetonide methyls), 16.5 (q, allylic CH_3), 13.5 (q, angular CH_3), 13.5 (two q, amide methyls). Purification of a small portion by collection from analytical HPLC (15% ethyl acetate in hexane, 2.0 mL/min, t_R 3.0 column volumes) and recrystallization from hexane gave pure **27** (mp 85–87 °C) as colorless needles; MS 309 (2), 294 (9), 281 (1), 252 (5), 251 (39), 223 (2), 208 (10), 180 (2), 156 (28), 155 (7), 151 (45), 140 (9), 123 (30), 122 (10), 109 (4), 100 (79), 95 (17), 85 (4), 83 (31), 81 (5), 72 (70), 70 (11), 69 (13), 67 (10), 58 (44), 57 (12), 56 (30), 55 (33), 44 (52), 43 (100), 42 (19), 41 (42), 40 (19), 39 (24); $[\alpha]^{25}_D$ +173.0° (*c* 0.18, CH_2Cl_2). Anal. Calcd for $C_{17}H_{27}O_4N$: C, 65.99; H, 8.80; N, 4.53. Found: C, 66.09; H, 8.77; N, 4.48.

X-ray.[34] A single crystal of $C_{17}H_{27}NO_4$, which measured ~0.2 × 0.4 × 0.5 mm, was mounted on a glass fiber. Preliminary examination on a Syntex P$\bar{1}$ diffractometer showed the crystal to be orthorhombic, $P2_12_12_1$. The unit cell parameters (at 19 ± 1 °C, λ Mo K$\bar{\alpha}$ = 0.71073 Å) are a = 8.721 (5), b = 10.350 (4), and c = 19.641 (8)°. These parameters were determined by a least-squares refinement utilizing the setting angles of 30 reflections (17° < 2θ < 22°) each centered at ±2θ. The calculated density is 1.16 g/cm^3 for Z = 4.

Intensity data were collected by using θ–2θ scans from 0.8° below Kα to 0.8° above Kα_2 and scan ratios varying from 2.0 to 24.0 determinations/min. Four standard reflections were measured every 50 reflections to monitor the long-term stability. The intensities of the standard reflections showed no systematic changes during the time required to collect the data. The intensity data were reduced and standard deviations calculated as described previously.[51] The 719 data with $F_o > 3\theta(F_o)$ were retained as observed and utilized for the solution and refinement of the structure (36% of the theoretical number possible).

The structure was solved by direct methods utilizing the MULTAN[52] package and was refined by full-matrix least-squares techniques. A difference electron density map revealed most of the hydrogen atom positions. Hydrogen atoms were then included in the model in idealized positions (C–H = 1.0 Å; B(H) = B(C) + 1.0). The full isotropic refinement was then carried to convergence. The final value of $R_1 = \sum||F_o| - |F_c||/\sum F_o$ was 0.14; that of $R_2 = [\sum\omega(|F_o| - |F_c|)^2/\sum\omega(F_o)^2]^{1/2}$ was 0.17. The estimated standard deviation of an observation of unit weight was 3.59. The final difference electron density map was judged to be free of significant features.

See Appendix for data tables and ORTEP drawing. The mixture of cyclopentanones was separated by collection from analytical HPLC (5% ethyl acetate in hexane, 2.0 mL/min) to yield pure *N,N*-diethyl-2(*S*)-carboxamido-4(*S*),5(*S*)-(isopropylidenedioxy)-2(*S*)-methyl-3(*S*)-[(*E*)-propenyl]cyclopentanone (**28**, 16.4 mg, 11%, t_R 8.0 column volumes) and *N,N*-diethyl-2(*R*)-carboxamido-4(*S*),5(*S*)-isopropylidene-2(*R*)-methyl-3(*S*)-[(*E*)-propenyl]cyclopentanone (**29**, 14.6 mg, 10%, t_R 6.4 column volumes) as colorless oils.

28: ^1H NMR (270 MHz, $CDCl_3$) 1.12 (m, 6 H), 1.20 (s, 3 H), 1.35 (s, 3 H), 1.50 (s, 3 H), 1.71 (dd, 3 H, J = 6.6, 1.5 Hz), 3.22 (m, 1 H), 3.34 (m, 4 H), 4.55 (d, 1 H, J = 6.6 Hz), 4.67 (dd, 1 H, J = 6.6, 4.4 Hz), 5.24 (ddq, 1 H, J = 15, 9, 1.5 Hz), 5.64 (dqd, 1 H, J = 15, 6.6, 0.9 Hz); IR ($CDCl_3$) 2980, 2920, 1765, 1630, 1625, 1455, 1425, 1370, 1270, 1210, 1150, 1075, 1050, 970 cm^{-1}; ^{13}C NMR (50.1 MHz, $CDCl_3$) 208.6 (s), 168.3 (s), 130.3 (d), 125.8 (d), 113.9 (s), 80.1 (d), 78.4 (d), 61.1 (s), 51.6 (d), 41.8 (t), 40.6 (t), 26.3 (q, acetonide methyls), 18.5 (q, angular CH_3), 18.1 (q, vinyl CH_3), 12.8 and 12.7 (q, amide methyls); MS 309 (7), 294 (0.5), 281 (2), 223 (4), 194 (6), 182 (11), 171 (4), 151 (7), 134 (2), 129 (2), 123 (5), 109 (16), 100 (100), 83 (15), 81 (19), 72 (41), 71 (12), 59 (10), 58 (23), 55 (9), 44 (18), 43 (31), 41 (18); $[\alpha]^{25}_D$ +33.8° (*c* 0.74, CH_2Cl_2). Anal. Calcd for $C_{17}H_{27}O_4N$: C, 65.99; H, 8.80; N, 4.53. Found: C, 66.09; H, 8.83; N, 4.46.

29: ^1H NMR (270 MHz, $CDCl_3$): 1.11 (m, 6 H), 1.35 (s, 3 H), 1.45 (s, 3 H), 1.46 (s, 3 H), 1.73 (d, 3 H, J = 4.8 Hz), 2.46 (dd, 1 H, J = 8.5, 6.0 Hz), 3.08 (m, 2 H), 3.43 (m, 2 H), 4.67 (dd, 1 H, J = 7.2, 6.0 Hz), 4.85 (d, 1 H, J = 7.2 Hz), 5.69 (m, 2 H); IR ($CDCl_3$) 1765, 1625, 1600, 1460, 1430 cm^{-1}; ^{13}C NMR (50.1 MHz, $CDCl_3$) 208.4 (s), 170.3 (s), 130.2 (d), 128.0 (d), 113.9 (s), 80.0 (d), 79.9 (d), 63.2 (s), 57.7 (d), 41 (two t), 27.1 and 25.3 (q, acetonide methyls), 19.1 (q, angular CH_3), 18.1 (q, vinyl CH_3), 12.7 (q, amide methyls); MS 309 (24), 294 (3), 281 (1), 251 (2), 223 (2), 194 (14), 182 (60), 171 (4), 166 (5), 151 (3), 123 (5), 109 (24), 100 (100), 85 (14), 83 (10), 72 (27), 58 (9), 55 (10), 44 (20), 43 (31), 41 (18); $[\alpha]^{25}_D$ +7.9° (*c* 0.68, CH_2Cl_2). Anal. Calcd for $C_{17}H_{27}O_4N$: C, 65.99; H, 8.80; N, 4.53. Found: C, 66.10; H, 8.79; N, 4.51.

Method C (Table I, entry 2). Several experiments were performed in which $(Ph_3P)_4Pd$ (6–22 mol %) was added to a stirred solution of **20** in dry, deoxygenated Me_2SO (0.2 M) at 25 °C under argon and the solution heated at 60–130 °C for 9–47 h. TLC purification of these combined reaction mixtures, using two elutions with 50% ethyl acetate in hexane (v/v), yielded pure **20** (73%, R_f 0.4), pure **26** (20%, R_f 0.6), pure **27** (6%, R_f 0.75), and an impure compound tentatively identified as *N,N*-diethyl-(*E*)-2-[2(*S*),3(*S*)-(isopropylidenedioxy)-5(*S*)-[(*E*)-propenyl)tetrahydrofuran-2-ylidene]propionamide (1%, R_f 0.5) as a yellow oil: NMR (270 MHz, $CDCl_3$) 1.15 (t, 6 H, J = 7 Hz), 1.30 (s, 3 H), 1.50 (s, 3 H), 1.71 (dd, 3 H, J = 6.5, 1.6 Hz), 1.85 (d, 3 H, J = 0.5 Hz), 3.3 (m, 2 H), 3.5 (m, 2 H), 4.47 (ddd, 1 H, J = 6.2, 2.2, 1.0 Hz), 4.71 (ddd, 1 H, J = 7.5, 2.2, 1.6 Hz), 5.20 (d, 1 H, J = 6.2 Hz), 5.40 (ddq, 1 H, J = 15.2, 7.5, 1.6 Hz), 5.78 (dqd, 1 H, J = 15.2, 6.5, 1.0 Hz); IR ($CDCl_3$) 1695, 1605, 1440, 1370 cm^{-1}.

Preparation of 2(*S*)-Carbo-*tert*-butoxy-6(*S*),7(*S*)-isopropylidenedioxy-3(*R*)-methylcyclohept-4-enone (32). Enol ether **21b** (50.7 mg, 0.17 mmol) (**21a** produces identical results) and $(dppe)_2Pd$ (9.5 mg, 0.01 mmol) were combined in a dry NMR tube and dissolved in 0.5 mL dry, deoxygenated Me_2SO at 100 °C under argon. After 10 min the NMR spectra indicated **21b** was consumed. The reaction mixture was cooled, and TLC purification, using 50% ethyl acetate in hexane, yielded pure **32** (32.3 mg, 64%, R_f 0.6) as a clear colorless oil: ^1H NMR (270 MHz, $CDCl_3$) 1.17 (d, 3 H, J = 6.1 Hz), 1.42 (s, 3 H), 1.46 (s, 9 H), 1.60 (s, 3 H), 3.07 (quintet of t, 1 H, J = 6.1, 1.8 Hz) [sequential irradiation at 1.14, 3.18, 5.19, 5.51 and 5.78 show 3.07 (dqddd, 1 H, J = 12.1, 6.1, 6.0, 1.9, 1.7 Hz)], 3.18 (d, 1 H, J = 12.1 Hz), 5.19 (ddt, 1 H, J = 8.3, 2.2, 1.8 Hz) [sequential irradiation at 3.07, 5.40, 5.51, and 5.78 show 5.19 (dddd, 1 H, J = 8.3, 2.2, 1.9, 1.7 Hz)], 5.40 (d, 1 H, J = 8.3 Hz), 5.51 (ddd, 1 H, J = 10.8, 6.0, 2.2 Hz), 5.78 (dt, 1 H, J = 10.8, 1.9 Hz); IR ($CDCl_3$) 1740, 1715, 1455, 1380, 1370 cm^{-1}. A portion was purified by collection from analytical HPLC (5% ethyl acetate in hexane, 2.0 mL/min, t_R 2.6 column volumnes): ^{13}C NMR (50.1 MHz, $CDCl_3$) 199.5 (s), 166.8 (s), 134.0 (d), 129.8 (d), 109.8 (s), 82.7 (s), 80.6 (d), 76.0 (d), 68.2 (d), 32.1 (d), 28.0 (q, ester methyls), 26.5 and 25.1 (q, acetonide methyls), 18.3 (q, allylic methyl); MS 196 (0.5), 181 (1), 154 (2), 138 (2), 119 (2), 119 (2), 109 (3), 97 (3), 95 (2), 81 (13), 69 (10), 68 (18), 58 (13), 57 (26), 56 (12), 44 (100), 43 (79), 41 (50), 40 (19), 39 (11); $[\alpha]^{25}_D$ +178.5° (*c* 1.18, CH_2Cl_2). Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84;

(51) Haller, K. J.; Enemark, J. H. *Inorg. Chem.* **1978**, *17*, 3552.
(52) Germain, G.; Main, P.; Woolpon, M. M. *Acta Crystallogr., Sect. A* **1971**, *27*, 368.

H, 8.16. Found: C, 64.63; H, 8.01.

Preparation of *tert*-Butyl (*E*)-[2(*S*),3(*S*)-(Isopropylidenedioxy)-5-(*S*)-[(*E*)-propenyl]tetrahydrofuran-2-ylidene]acetate (33). To a stirred solution of **21b** (51.1 mg, 0.17 mmol) in 0.8 mL of dry THF at 25 °C under argon was added $(dppe)_2Pd$ (9.1 mg, 0.01 mmol). The clear yellow solution was stirred at 25 °C for 2 h and 50 °C for 5 h. The solvent was removed in vacuo, and TLC purification, using two elutions of 30% acetone in hexane (v/v), yielded **33** (24.2 mg, 47%, R_f 0.5) which was pure by NMR spectroscopy and analytical TLC: ^{1}H NMR (270 MHz, $CDCl_3$) 1.38 (s, 3 H), 1.41 (broad s, 12 H), 1.69 (dm, 3 H, J = 6.5 Hz), 4.52 (dd, 1 H, J = 5.9, 1.7 Hz), 4.82 (dm, 1 H, J = 6.7 Hz), 5.33 (ddq, 1 H, J = 15.3, 6.7, 1.7 Hz), 5.35 (d, 1 H, J = 1.2 Hz), 5.64 (dd, 1 H, J = 5.9, 1.2 Hz), 5.77 (dqd, 1 H, J = 15.3, 6.5, 1.0 Hz); IR ($CDCl_3$) 2980, 2920, 2860, 1695, 1655, 1450, 1370, 1315, 1265, 1220, 1160, 1120, 1085, 1010, 970, 855 cm^{-1}; ^{13}C NMR (50.1 MHz, $CDCl_3$) 170.5 (s), 166.2 (s), 130.3 (d), 126.9 (d), 113.2 (s), 96.9 (s), 87.2 (d), 82.5 (s), 79.8 (d), 79.1 (d), 28.3 (q, ester methyls), 27.0 and 25.9 (q, acetonide methyls), 17.7 (q, vinyl methyl).

Preparation of 2(*S*),3(*S*)-(Isopropylidenedioxy)-4(*R*)-[(*Z*)-propenyl]cyclopentanone (31). To enol ether **21a** (85.5 mg, 0.29 mmol) and polymer-supported palladium catalyst[36] (45.7 mg, 0.02 mmol Pd) at 25 °C under argon was added 1.1 mL of dry, deoxygenated toluene. Distilled *O,N*-bis(trimethylsilyl)acetamide (240.0 mg, 1.18 mmol) was added, and the mixture was allowed to stand at 25 °C for 1 h to allow the polymer beads to swell. The mixture was heated to reflux, stirred occasionally over 2 h, and cooled to 25 °C. The yellow solution was decanted from the polymer beads; the beads were washed with toluene (10 × 0.5 mL), and the washings were combined with the solution. The solvent was removed in vacuo (0.02 mm) to give a yellow oil (106.2 mg). Proton NMR and analytical HPLC (8% ethyl acetate in hexane, 2.0 mL/min) analyses showed this oil to contain trace amounts of hydrolyzed *O,N*-bis(trimethylsilyl)acetamide, 58–60% of enol silyl ether **35**, 36–38% of **30**, 1% of cycloheptenone **32**, and 0–4% of decarboalkoxylated cyclopentanone **31**. This oil was dissolved in 0.65 mL of distilled, moist Me_2SO-d_6 in an NMR tube and heated at 70 °C for 7.5 h. TLC purification, using 50% acetone in hexane (v/v), yielded pure **31** (46.6 mg, 82%) as an off-white crystalline solid and another portion (11.0 mg, 80% pure) as a pale yellow oil: ^{1}H NMR (270 MHz, $CDCl_3$) 1.28 (s, 3 H), 1.36 (s, 3 H), 1.63 (dd, 3 H, J = 6.5, 1.4 Hz), 2.27 (A of ABX, 1 H, J = 18.4, 11.2 Hz), 2.37 (B of ABX, 1 H, J = 18.4, 9.4 Hz), 3.13 (x of ABX, 1 H, J_{AX} = 11.2 Hz, J_{BX} = 9.4 Hz), 4.16 (d, 1 H, J = 4.3 Hz), 4.63 (t, 1 H, J = 4.3 Hz), 5.48 (ddq, 1 H, J = 11.0, 10.6, 1.4 Hz), 5.62 (dqd, 1 H, J = 10.6, 6.5, 0.8 Hz); IR ($CDCl_3$): 1755, 1385, 1375 cm^{-1}; ^{13}C NMR (50.1 MHz, $CDCl_3$) 213.5 (s), 127.6 (d), 126.7 (d), 112.3 (s), 80.0 (d, acetonide methines), 39.4 (t), 32.9 (d), 26.6 and 24.9 (q, acetonide methyls), 13.2 (q, vinyl methyl). A portion was recrystallized from hexane to give colorless needles (mp 70–71 °C): MS 197 (3), 196 (27), 181 (16), 167 (16), 159 (10), 153 (10), 139 (31), 138 (38), 123 (20), 121 (11), 110 (22), 109 (32), 101 (29), 100 (66), 97 (32), 96 (17), 95 (63), 93 (18), 85 (67), 83 (14), 82 (37), 81 (96), 80 (11), 79 (40), 77 (20), 69 (61), 68 (88), 67 (71), 66 (22), 65 (18), 60 (18), 59 (60), 57 (12), 55 (48), 54 (20), 53 (57), 52 (10), 51 (14), 44 (11), 43 (100), 42 (48), 41 (80), 40 (42), 39 (72) (calcd for $C_{11}H_{16}O_3$, 196.1099; found, 196.1104); $[\alpha]^{25}_D$ +127.3° [c 1.92, CH_2Cl_2]). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.42; H, 8.14.

Preparation of 2(*S*)-Carbo-*tert*-butoxy-4(*S*),5(*S*)-(isopropylidenedioxy)-5(*R*)-[(*Z*)-propenyl]cyclopentanone (30) and Carbo-*tert*-butoxy-3(*S*),4(*S*)-(isopropylidenedioxy)-5(*R*)-[(*Z*)-propenyl]-2-(trimethylsiloxy)cyclopentanone (35). To enol ether **21a** (157.1 mg, 0.53 mmol) (**21b** produces identical results) and phosphinylated polystyrene supported palladium catalyst[36] (62% of phenyl rings substituted by PPh_2, 2% cross-linked, 73.96% C, 5.54% H, 5.75% P, 3.76% Pd, 46.8 mg, 0.02 mmol of Pd) at 25 °C under argon was added 2.2 mL of dry, deoxygenated toluene. Distilled *O,N*-bis(trimethylsilyl)acetamide (268.8 mg, 1.32 mmol) was added, and the mixture was allowed to stand at 25 °C for 1 h to allow the polymer beads to swell. The mixture was heated to reflux and stirred occasionally over 10 h and cooled to 25 °C. The yellow solution was decanted from the polymer beads; the beads were washed with toluene (5 × 2 mL), and the washings were combined with the solution. The resultant solution was concentrated in vacuo (0.02 mm) to give a yellow oil (157.2 mg). Proton NMR and analytical HPLC analysis [8% ethyl acetate in hexane (v/v), 2.0 mL/min, t_R 1.4 column volumes] showed this oil to contain small amounts of hydrolyzed *O,N*-bis(trimethylsilyl)acetamide and 95% of enol silyl ether **35**: NMR (270 MHz, $CDCl_3$) 0.32 (s, 9 H), 1.35 (s, 3 H), 1.45 (broa d s, 12 H), 1.72 (dd, 3 H, J = 7, 1.8 Hz), 3.81 (ddd, 1 H, J = 10.5, 6.1, 0.8 Hz), 4.63 (t, 1 H, J = 6.1 Hz), 4.73 (d, 1 H, J = 6.1 Hz), 5.35 (ddq, 1 H, J = 11, 10.5, 1.8 Hz), 5.63 (dqd, 1 H, J = 11, 7, 0.8 Hz); IR ($CDCl_3$) 1705, 1630, 1365 cm^{-1}. TLC purification, using three elutions with 20% acetone in hexane (v/v), yielded a significant amount of decarboalkoxylated product and **30**, which exists as a 64:36 keto enol mixture (61.0 mg, 39%) which was pure by NMR and analytical TLC/HPLC: ^{1}H NMR (270 MHz, $CDCl_3$) (keto form) 1.35 (s, 3 H), 1.45 (broad s, 12 H), 1.72 (dd, 3 H, J = 6.7, 1.7 Hz), 3.36 (d, 1 H, J = 12.1 Hz), 3.56 (ddd, 1 H, J = 12.1, 9.5, 4.0, 0.7 Hz), 4.32 (d, 1 H, J = 5.0 Hz), 4.70 (dd, 1 H, J = 5.0, 4.0 Hz), 5.53 (ddq, 1 H, J = 10.5, 9.5, 1.7 Hz), 5.76 (dqd, 1 H, J = 10.5, 6.7, 0.7 Hz); (enol form) 1.35 (s, 3 H), 1.45 (broad s, 12 H), 1.72 (dd, 3 H, J = 6.7, 1.7 Hz), 3.79 (ddd, 1 H, J = 10.2, 6.1, 0.6 Hz), 4.67 (t, 1 H, J = 6.1 Hz), 4.95 (d, 1 H, J = 6.1 Hz), 5.35 (ddq, 1 H, J = 10.9, 10.2, 1.7 Hz), 5.63 (dqd, 1 H, J = 10.9, 6.7, 0.6 Hz); IR ($CDCl_3$) 3250, 2980, 2930, 1765, 1720, 1665, 1655, 1450, 1370, 1350, 1250, 1210, 1150, 1070 cm^{-1}; ^{13}C NMR (50.1 MHz, $CDCl_3$) (keto form) 206.4 (s), 167.4 (s), 128.3 (d), 126.0 (d), 112.6 (s), 82.1 (s), 79.9 (d), 78.6 (d), 57.1 (d), 37.4 (d), 28.0 (q, ester methyls), 26.7 and 24.8 (q, acetonide methyls), 13.4 (q, vinyl methyl); (enol form) 169.8 (s), 169.4 (s), 134.2 (d), 124.9 (s), 111.7 (s), 104.4 (s), 80.9 (s), 77.4 (s), 76.0 (s), 39.3 (d), 31.2 and 25.5 (q, acetonide methyls), 28.2 (q, ester methyls), 13.3 (q, vinyl methyl); MS 281 (0.5), 240 (1), 225 (1), 223 (4), 212 (1), 196 (2), 195 (3), 194 (3), 193 (3), 182 (5), 181 (2), 138 (8), 137 (7), 136 (6), 135 (5), 123 (6), 110 (5), 109 (12), 100 (66), 97 (10), 95 (46), 85 (33), 81 (58), 79 (14), 69 (12), 68 (44), 67 (22), 66 (7), 60 (5), 59 (100), 57 (96), 56 (13), 55 (14), 53 (12), 44 (33), 43 (89), 41 (70), 40 (7), 39 (20); $[\alpha]^{25}_D$ +63.5° (c = 3.22, CH_2Cl_2). Anal. Calcd for $C_{16}H_{24}O_5$: C, 64.84; H, 8.16. Found: C, 65.03; H, 8.18.

Preparation of 2-(Carbomethoxy)-3-(3-bromo-5,6-dihydronaphth-7-yl)cyclopentane (37). To a stirred solution of enol ether **6**[17] (207.0 mg, 0.59 mmol) in dry Me_2SO (2.6 mL, previously deoxygenated by bubbling argon) at 65 °C under argon was added $Pd(dppe)_2$ (28.9 mg, 0.03 mmol). The resulting clear, yellow solution was stirred at 65 °C for 1.5 h, the solvent was removed in vacuo at 25 °C, and the residue was purified by TLC, using three elutions with 30% acetone in hexane (v/v), to yield **37** (168.6 mg, R_f 0.6, 81%) as a pale yellow solid (mp 110–118 °C), which was recrystallized from absolute ethanol to give colorless needles (mp 117–119 °C). Proton NMR proved these to be an *E*:*Z* mixture of 96:4: ^{1}H NMR (270 MHz, $CDCl_3$) 1.7–1.9 (m, 1 H), 2.3–2.6 (m, 5 H), 2.80 (t, 2 H, J = 8 Hz), 3.26 (d, 1 H, J = 11.5 Hz), 3.39 (td, 1 H, J = 11.5, 6.2 Hz), 3.69 (s, 0.12 H), 3.76 (s, 2.88 H), 6.14 (bs, 0.04 H), 6.28 (bs, 0.06 H), 6.88 (d, 1 H, J = 7.5 Hz), 7.25 (m, 2 H); IR ($CDCl_3$) 1765, 1725, 1655, 1620, 1590 (w), 1480, 1440, 1410, 1360, 1330 cm^{-1}; ^{13}C NMR (C_6D_6) 209, 169, 141, 137, 133, 130, 127.5, 127.5, 122, 120, 59, 52, 48, 38, 28, 26, 25; MS 350 (4), 348 (4), 318 (4), 316 (4), 291 (7), 289 (10), 258 (3), 256 (3), 234 (2), 232 (2), 221 (1), 219 (2), 208 (3), 206 (2), 181 (2), 179 (1), 170 (6), 168 (1), 167 (3), 166 (3), 165 (2), 154 (3), 153 (6), 152 (4), 151 (1), 143 (3), 141 (5), 128 (5), 125 (11), 97 (45), 95 (5), 86 (72), 84 (100), 85 (18), 83 (29), 77 (14), 71 (11), 69 (17), 57 (24), 56 (26), 55 (21), 49 (18), 47 (31), 45 (12), 44 (56), 43 (40), 41 (32), 40 (26), 36 (31) (calcd for $C_{17}H_{17}{}^{79}BrO_3$, 348.0361; found, 348.0354). UV (5.4 × 10^{-5} M in MeOH) 271 (ϵ 17,040), 279 (17,960), 291 (11,110). Anal. Calcd for $C_{17}H_{17}BrO_3$: C, 58.46; H, 4.91; Br, 22.88. Found: C, 58.59; H, 5.01; Br, 22.73.

Impurity bands (R_f 0.7) were collected from several similar experiments and repurified by TLC, using three elutions with 20% acetone in hexane (v/v), to yield a trace of **39** as a clear, pale yellow oil, which ^{1}H and ^{13}C NMR proved to be a 2:1 isomeric mixture: ^{1}H NMR (270 MHz, $CDCl_3$) 2.2–2.8 (m, 8 H), 3.2–2.2 (m, 0.33 H), 3.28 (d, 0.67 H, J = 10.6 Hz), 3.45 (s, 1 H), 3.54 (s, 2 H), 3.98 (m, 0.33 H), 4.52 (bd, 0.67 H, J = 10.6 Hz), 5.61 (bt, 0.67 H, J = 7.0 Hz), 5.75 (bt, 0.33 H, J = 7.0 Hz), 6.92 (d, 0.67 H, J = 8.0 Hz), 7.04 (d, 0.33 H, J = 8.0 Hz), 7.21 (m, 2 H); IR ($CDCl_3$) 2960, 2900, 2840, 1740, 1715, 1650, 1600, 1435, 1325, 1250, 1220, 1190, 1160, 1120, 1020, 820 cm^{-1}; ^{13}C NMR (minor isomer, C_6D_6) 204.0, 168.4, 141.5, 138.8, 135.8, 131.5, 129.9, 125.7, 123.9, 120.2, 67.3, 51.2, 40.1, 39.0, 33.5, 29.9, 24.0; (major isomer, C_6D_6) 202.4, 169.0, 141.6, 139.6, 136.1, 131.5, 129.9, 125.7, 123.7, 121.0, 68.5, 51.7, 41.6, 38.8, 33.1, 28.9, 22.7; MS 350 (0.6), 348 (0.6), 322 (0.7), 320 (0.8), 318 (0.5), 316 (0.5), 291 (1), 289 (1), 262 (2), 234 (2), 232 (2), 169 (2), 168 (2), 167 (2), 166 (1), 165 (2), 154 (2), 152 (1), 122 (7), 121 (77), 119 (2), 105 (5), 101 (3), 99 (3), 91 (6), 87 (3), 85 (10), 83 (18), 77 (8), 73 (7), 71 (23), 69 (11), 67 (6), 59 (12), 58 (15), 57 (24), 55 (28), 45 (16), 44 (14), 43 (100), 42 (8), 41 (25) (calcd for $C_{17}H_{17}{}^{79}BrO_3$, 348.0361; found, 348.0368); UV (9.4 × 10^{-4} M in MeOH) 258 (ϵ 1600), 263 (1700), 270 (1600).

Preparation of (*E*)-2-(Carbomethoxy)-2-(carbo-*tert*-butoxymethyl)-3-(3-bromo-5,6-dihydronaphth-7-yl)cyclopentanone (38). To a stirred mixture of β-keto ester **37** (380.6 mg, 1.09 mmol) and anhydrous K_2CO_3 (451.2 mg, 3.27 mmol) in 5.3 mL dry acetone at 35 °C was added *tert*-butyl iodoacetate (351.3 mg, 1.44 mmol). The mixture was stirred at 35 °C for 4 h and partitioned between ether (30 mL) and water (20 mL). The aqueous phase was extracted with ether (30 mL), and the combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated in vacuo. TLC purification, using two elutions

of 30% acetone in hexane (v/v), yielded the O-alkylation product (65.6 mg, R_f 0.5, 13%) as a pale yellow gum, and C-alkylation product **38** (434.2 mg, R_f 0.6, 86%) also as a pale yellow gum, which was pure by analytic TLC and NMR.

38: ^{1}H NMR (270 MHz, $CDCl_3$) 2.04–2.16 (m, 2 H), 2.28–2.56 (m, 2 H), 2.63 (dd, 2 H, J = 10.2, 8.0 Hz), 2.75 (t, 2 H, J = 8.0 Hz), 2.93 (d, AB pattern, 1 H, J = 17.5 Hz), 3.17 (d, AB pattern, 1 H, J = 17.5 Hz), 3.35 (dd, 1 H, J = 11.6, 6.1 Hz), 3.57 (s, 3 H), 6.27 (bs, 1 H), 6.86 (d, 1 H, J = 8.0 Hz), 7.26 (m, 2 H), 6.27 (bs, 1 H), 6.86 (d, 1 H, J = 8.0 Hz), 7.26 (m, 2 H), 6.27 (bs, 1 H), 6.86 (d, 1 H, J = 8.0 Hz), 7.26 (m, 2 H); IR ($CDCl_3$) 2940, 2860, 2820, 1755, 1725, 1720, 1640 (w), 1590, 1480, 1430, 1410, 1370, 1310, 1220, 1155, 1080, 970, 880, 850, 820; ^{13}C NMR ($CDCl_3$) 213.0, 169.8, 169.7, 139.0, 137.0, 132.8, 130.0, 129.3, 127.2, 123.8, 120.1, 81.3, 61.4, 52.0, 50.4, 38.1, 37.6, 28.0, 27.8, 27.0, 23.3; MS 408 (7), 406 (8), 390 (7), 388 (6), 359 (3), 357 (2), 331 (7), 329 (8), 234 (3), 232 (2), 170 (4), 169 (2), 149 (3), 141 (3), 128 (3), 119 (2), 94 (4), 86 (34), 84 (53), 77 (14), 69 (10), 59 (10), 58 (39), 57 (54), 56 (14), 55 (18), 49 (10), 47 (12), 44 (14), 43 (100), 41 (33) [calcd for $C_{19}H_{19}{}^{79}BrO_5$ (M – C_4H_8), 406.0416; found, 406.0405]. Anal. Calcd for $C_{23}H_{27}BrO_5$: C, 59.62; H, 5.87; Br, 17.25. Found: C, 59.73; H, 5.93; Br, 17.40.

Preparation of (*E*)-2-(Carbomethoxy)-3-[(*E*)-3-(1-ethoxyethoxy)-oct-1-en-1-yl]cyclopentanone (42). To a stirred solution of distilled (*E*)-**16** (49.0 mg, 0.14 mmol) and distilled *O,N*-bis(trimethylsilyl)acetamide (116.8 mg, 0.5, mmol) in 0.7 mL of dry, deoxygenated Me_2SO at 25 °C under argon was added $(dppe)_2Pd$ (9.2 mg, 0.01 mmol). The slurry was placed in a 100 °C oil bath and stirred for 3 h. The catalyst dissolved in 3 min, and the yellow solution gradually darkened to clear red. The reaction mixture was cooled to 25 °C, and preparative TLC purification, using two elutions with 50% acetone in hexane (v/v), yielded **42** (36.3 mg, 74%, R_f 0.65), which was pure by analytical TLC and ^{1}H NMR, and proven by ^{13}C NMR to be a mixture of at least two diastereomers. Undistilled (*E*)-**16** (67.3 mg, 0.20 mmol) underwent the same reaction in refluxing dioxane (0.7 mL) with *O,N*-bis(trimethylsilyl)-acetamide (160.8 mg, 0.80 mmol) for 16 h to provide **42** in 67%, but much more $Pd(dppe)_2$ (56.3 mg, 0.06 mmol) was required. Undistilled (*Z*)-**16**, when subjected to either of the above conditions, was found to rearrange first to (*E*)-**16** and then proceed to **42** in 68% with 12% $Pd(dppe)_2$: NMR (270 MHz, $CDCl_3$) 0.88 (broad t, 3 H, J = 6.0 Hz), 1.17 (t, 1.5 H, J = 6.5 Hz), 1.19 (t, 1.5 H, J = 6.5 Hz), 1.29 (d, 1.5 H, J = 5.2 Hz), 1.2–1.3 (m, 8 H), 1.3–1.7 (m, 2 H), 2.25 (m, 0.5 H), 2.41 (m, 1.5 H), 3.00 (d, 1 H, J = 11.2 Hz), 3.22 (dddd, 1 H, J = 11.2, 6.0, 5.2, 1.5 Hz), 3.3–3.7 (m, 2 H), 3.67 (s, 0.3 H), 3.74 (s, 2.7 H), 3.84 (q, 0.25 H, J = 7.5 Hz), 3.86 (q, 0.25 H, J = 7.5 Hz), 3.98 (nq, 0.50 H, J = 7.5 Hz), 4.65 (q, 0.5 H, J = 5.2 Hz), 4.69 (q, 0.5 H, J = 5.2 Hz), 5.42 (dd, 0.5 H, J = 16.2, 7.5 Hz), 5.59 (m, 1.5 H); IR ($CDCl_3$) 1760, 1730, 1220, 1380, 1340 cm^{-1}; MS (30 eV) 340 (0.0), 270 (0.8), 191 (2), 165 (3), 162 (3), 161 (10), 148 (2), 119 (2), 118 (2), 117 (2), 109 (3), 105 (4), 93 (4), 92 (4), 91 (10), 79 (14), 77 (11), 73 (100), 67 (5), 65 (3), 55 (11), 53 (5), 51 (4), 45 (56), 44 (94), 43 (30), 41 (19), 40 (75), 39 (11) (calcd for $C_{19}H_{32}O_5$, 340.2250; found: 340.2248); ^{13}C NMR (50.1 MHz, $CDCl_3$) 210.3 (s), 168.9 (s), [133.4, 132.7 (d)], [132.4, 130.9 (d)], [98.7, 96.8 (d)], [76.7, 76.2 (d)], 61.1 (d), [60.9, 59.0 (d)], 52.4 (q), [43.8, 43.6 (d)], 38.1 (t), 35.6 (t), 31.7 (t), 27.6 (t), [25.0, 24.8 (t)], 22.6 (t), [20.6, 20.4 (q)], [15.4, 15.2 (q)], 14.0 (q).

Preparation of (*E*)-2-(Carbomethoxy)-3-[(*E*)-3-hydroxyoct-1-en-1-yl]cyclopentanone (41). To a stirred solution of protected cyclopentanone **42** (32.2 mg, 0.10 mmol) in 0.2 mL distilled THF at 20 °C under nitrogen was added a solution of 65% (v/v) acetic acid in water (1.9 mL). The colorless solution was stirred at 20 °C for 8 h and at 30 °C for 3 h, diluted with ether (15 mL), and carefully neutralized with saturated aqueous $NaHCO_3$ solution (14 mL). The aqueous phase was extracted with ether (2 × 10 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (5 mL), dried (Na_2SO_4), and concentrated in vacuo to give essentially pure **41** (25.4 mg, 100%). Preparative TLC purification, using two elutions with 50% ethyl acetate in hexane (v/v), yielded **41** (21.3 mg, 84%) which was pure by analytical TLC and proven by ^{1}H NMR and ^{13}C NMR to be a mixture of two diastereomers: NMR (270 MHz, C_6D_6) 0.88 (t, 3 H, J = 6.8 Hz), 1.02 (m, 1 H), 1.1–1.5 (m, 9 H), 1.57 (m, 1 H), 1.85 (m, 1 H), 2.77 (d, 0.5 H, J = 12.0 Hz), 2.79 (d, 0.5 H, J = 12.0 Hz), 3.03 (dd, 0.5 Hz, J = 12.0, 6.6 Hz), 3.06 (dd, 0.5 H, J = 12.0, 6.6 Hz), 3.27 (s, 0.15 H), 3.28 (s, 0.15 H), 3.41 (s, 2.7 H), 3.88 (q, 0.5 H, J = 5.9 Hz), 3.90 (q, 0.5 H, J = 5.9 Hz), 5.40 (ddd, 1 H, J = 16.2, 6.6, 5.9 Hz); IR ($CHCl_3$) 3680, 3600, 3620–3400, 1760, 1730, 1460, 1440, 1410, 1340 cm^{-1}. MS (30 eV): 237 (1), 236 (1), 219 (4), 218 (4), 192 (7), 165 (6), 161 (6), 150 (8), 149 (8), 148 (19), 139 (17), 133 (6), 123 (7), 121 (12), 109 (24), 107 (11), 105 (12), 96 (23), 94 (18), 93 (33), 91 (26), 83 (18), 81 (17), 80 (21), 79 (73), 78 (12), 77 (26), 71 (12), 68 (11), 67 (10), 55 (53), 44 (100), 43 (47), 41 (42), 40 (36), 36 (13); ^{13}C NMR (50.1 MHz, $CDCl_3$) 210.5 (s), 169.2 (s), 134.8 (d), [130.5, 130.4 (d)], [72.4, 72.3 (d)], 61.2 (d), 52.4 (q), [43.7, 43.6 (d)], 38.1 (t), 37.3 (t), 31.7 (t), 27.6 (t), 25.0 (t), 22.6 (t), 14.0 (q). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 66.95; H, 8.86.

Preparation of 2-(Carbomethoxy)-3-(propen-2-yl)cyclopentanone (43). To a mixture of (*E*)-**15** (42.8 mg, 0.24 mmol) and $(dppe)_2Pd$ (13.2 mg, 0.01 mmol) in a dry NMR tube at 25 °C was added 0.6 mL dry, deoxygenated Me_2SO-d_6. The mixture was heated at 50–80 °C and agitated periodically over 10 h. Preparative TLC purification, using two elutions with 25% acetone in hexane (v/v), yielded pure **43** (27.0 mg, 63%) as a clear, pale yellow oil which was pure by analytical TLC and shown by ^{1}H NMR to be an *E*:*Z* (88:12) mixture: NMR (CCl_4) 1.5–1.95 (m, 1 H), 1.82 (s, 3 H), 1.95–2.8 (m, 3.2 H), 2.95–3.28 (m, 1.8 H), 3.70 (s, 3 H), 4.68 (bs, 0.24 H), 4.85 (bs, 1.76 H); IR (CCl_4) 1760, 1730, 1660, 1620, 1440, 1475, 1350 cm^{-1}.

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Supplementary Material Available: Fractional coordinates, selected interatomic distances and angles, and an ORTEP drawing of **27** (3 pages). Ordering information is given on any current masthead page.