(v) Stock solution (0.5 mL) and purified THF (1.5 mL) were refluxed for 2 h, maintained at ambient temperature for 12 h, and then refluxed for 2 h, all either under nitrogen or in air. Compound **8b** was unchanged.

(vi) Conditions were as for ii but 2 mg of DETAPAC was added prior to reflux. Compound **8b** was unchanged.

(vii) Conditions were as for iv but with the addition of 2 mg of DETAPAC. Quantitative conversion of **8b** to **9b** resulted.

X-ray Crystallography.[18] Single crystals of **3** and **9a** were prepared by the slow diffusion of hexane vapor into $CHCl_3$ solutions.

Crystal data for 9a: $C_{28}H_{34}N_2O_3S_3$; fw 542.79; triclinic, $P\bar{1}$, a = 10.456 (4) Å, b = 14.110 (2) Å, c = 10.404 (4) Å, α = 99.50 (2)°, β = 109.91 (3)°, γ = 99.11 (3)°, V = 1385 Å^3, Z = 2. Monochromatized Mo K_α radiation (λ = 0.71073 Å) was used. Data were collected for the index range $h,\pm k,\pm l$, on a CAD4F diffractometer[18a] using an ω-2θ scan to a 2θ limit of 50.00° at 23 °C. A total of 4735 unique data were collected, with 2666 observed with $I > 3\sigma(I)$. The structure was solved by direct methods.[18b] Final unweighted and weighted R values of 0.047 and 0.063, respectively, were obtained for 325 variables. The highest peak in the final difference Fourier was 0.37 (5) e Å^{-3} with no chemical significance.

Crystal data for 3: $C_{12}H_{22}N_2O_2S_2$; fws 290.45; monoclinic, $P2_1/c$, a = 9.163 (2) Å, b = 15.710 (6) Å, c = 10.635 (4) Å, β = 96.96 (2)°, V = 1520 Å^3, Z = 2. Monochromatized Mo K_α radiation (λ = 0.71073 Å) was used. Data were collected for the index range $h,k,\pm l$ on a CAD4F diffractometer[18a] using an ω-2θ scan to a 2θ limit of 54.00° at 23 °C. A total of 3442 unique data were collected, with 2435 observed at $I > 3\sigma(I)$. The structure was solved by direct methods.[18b] Final unweighted and weighted R values of 0.052 and 0.076, respectively, were obtained for 163 variables. The highest peak in the final difference Fourier was 0.42 (6) e Å^{-3} with no chemical significance.

Determination of Binding Constants to DNA. The relative binding constants of **2**, **5**, and naphtho[2,1-*b*]thiophene-3-carboxylic acid were estimated by displacement of intercalative binding of ethidium to calf thymus DNA and employing a value of $K_{assoc} = 1 \times 10^7$ M^{-1} at pH 7.0, 37 °C, and 40 mM NaCl for ethidium bound to calf thymus DNA.[19,20] It was determined that none of the compounds interferes with the fluorescence measurements, which were performed on a Turner 430 spectrofluorometer. The procedure, which involves following the displacement of the ethidium upon titrating in the drugs and determining the concentration of drug required to displace 50% of the ethidium, follows that of Morgan et al.[20] and gives relative rather than absolute values for binding constants. Higher concentrations of drugs displace all the ethidium from the DNA.

Acknowledgment. This investigation was supported by grants to J.W.L. from the National Cancer Institute of Canada and the Natural Sciences and Engineering Research Council of Canada. We thank Dr. Tom Nakashima and his colleagues for the high-field NMR measurements and Dr. Alan Hogg and his associates for the high-resolution mass spectra.

Registry No. 1, 115509-23-4; **2**, 115420-69-4; **3**, 115420-70-7; **4**, 115420-71-8; **5**, 115420-72-9; **6**, 108168-20-3; **7**, 115420-73-0; **8b**, 115420-74-1; **8d**, 115461-83-1; **8e**, 108168-12-3; **9a**, 115420-75-2; **9b**, 115420-76-3; **9c**, 115420-77-4; **9d**, 115420-78-5; naphtho[2,1-*b*]thiophene-3-carboxylic acid, 37094-53-4.

Supplementary Material Available: Positional and thermal parameters, derived hydrogen atom parameters, anisotropic thermal parameters, root-mean-square amplitudes of vibration, bond distances and angles, and torsion angles for **3** and **9a** (16 pages). Ordering information is given on any current masthead page.

(19) Le Pecq, J. B.; Paoletti, C. *J. Mol. Biol.* **1967**, *27*, 87.
(20) Morgan, A. R.; Lee, J. S.; Pulleyblank, D. E.; Murray, N. L.; Evans, D. H. *Nucleic Acids Res.* **1979**, *7*, 547.
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Preparation, Reactivity, and Spectral Properties of 1,3-Dioxin Vinylogous Esters: Versatile β-Ketovinyl Cation Equivalents†

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Received December 30, 1987

A full account of the preparation, reactivity, and spectral properties of three 1,3-dioxin vinylogous esters (**4**–**6**) is presented. The synthetic approach to these versatile β-ketovinyl cation equivalents involves a BF_3·Et_2O-promoted Prins reaction between cyclic 1,3-diketones (i.e., 1,3-cyclopentanedione, 1,3-cyclohexanedione, and 1,3-cycloheptanedione) and either formaldehyde or trioxane. The reactions explored include reductive and alkylative 1,3-ketone transpositions, affording a variety of simple β-unsubstituted and β-substituted α-hydroxymethyl α,β-enones, alkylations with carbon electrophiles, and hydroxylations with oxygen electrophiles.

Introduction

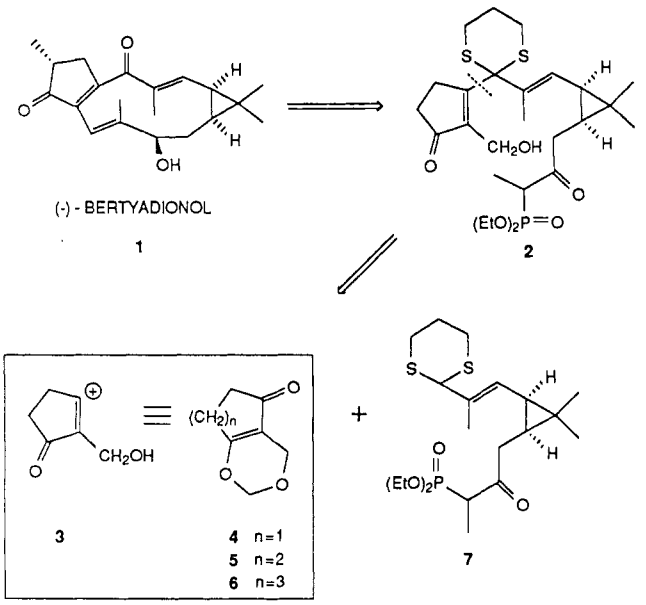
In connection with our recent synthesis of (−)-bertyadionol (**1**),[2] we required a versatile β-ketovinyl cation equivalent for α-(hydroxymethyl)cyclopentenone synthon **3**. Ideal in this regard appeared to be vinylogous ester **4**, wherein nucleophilic addition of the dianion of **7** to the carbonyl group of **4**, followed by an acidic workup would lead to enone **2** with concomitant loss of formaldehyde.[3]

As recently communicated, this tactic proved quite successful in that it permitted rapid assembly of the carbon skeleton of bertyadionol.[2] Having demonstrated the utility

† This paper is dedicated to Professor Harold W. Heine (Bucknell University) on the occasion of his 65th birthday.

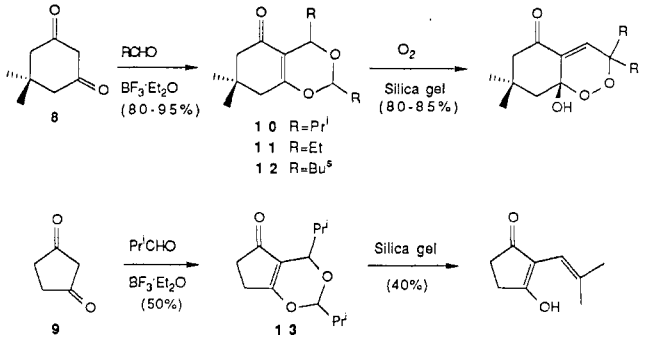
(1) National Institutes of Health (National Cancer Institute) Career Development Awardee, 1980–1985; J. S. Guggenheim Fellow, 1985–1986.
(2) Smith, A. B., III; Dorsey, B. D.; Visnick, M.; Maeda, T.; Malamas, M. S. *J. Am. Chem. Soc.* **1986**, *108*, 3110.
(3) For examples of alkylative 1,3-carbonyl transpositions in vinylogous esters, see: Corey, E. J.; Crouse, D. *J. Org. Chem.* **1968**, *33*, 298. Stork, G.; Danheiser, R. L. *J. Org. Chem.* **1973**, *38*, 1775. Quesada, M. L.; Schlessinger, R. H. *Synth. Commun.* **1976**, *6*, 555. Tobin, P. S.; Basu, S. K.; Grosserade, R. S.; Wheeler, D. M. S. *J. Org. Chem.* **1980**, *45*, 1250.

0022-3263/88/1953-4314$01.50/0



of **4** in at least one case, we decided to explore the chemistry of these 1,3-dioxin vinylogous esters in some depth. We report here a full account of that study; we note in advance that vinylogous ester **4** and the closely related six- and seven-membered analogues **5** and **6** hold considerable potential for the construction of both natural and unnatural carbocyclic products.[4]

The Prins Reaction of 1,3-Diketones with Formaldehyde: A General Approach to the 1,3-Dioxin Vinylogous Ester System. In 1982 Crow and co-workers,[5] in connection with the synthesis of plant-growth regulators, recorded the preparation of several substituted 1,3-dioxins (**10**–**13**). In particular, they observed that treatment of cyclic 1,3-diketones **8** and **9** with aliphatic aldehydes in the presence of BF_3·Et_2O led in good to excellent yield to substituted 1,3-dioxins. The resultant diastereomeric mixtures, however, were found to be inseparable, due in part to their propensity to rearrange and/or react with oxygen absorbed on silica gel.[5]



To account for the formation of the 1,3-dioxins, Crow proposed a mechanism (Scheme I) wherein the electron-rich enol of the 1,3-diketone attacks the BF_3–aldehyde complex in a Prins reaction.[6] Addition of a second equivalent of aldehyde, followed by cyclization, yields the dioxin. To ensure formation of the 1,3-dioxin ring, a slight excess of aldehyde (ca. 2.5–3.0 equiv) was employed.[5]

Scheme I

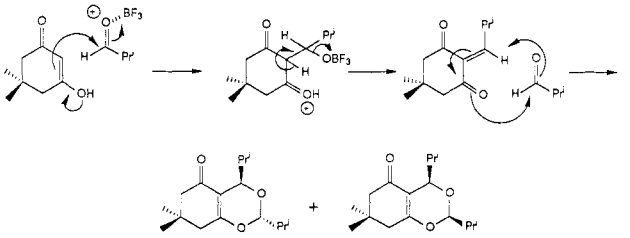
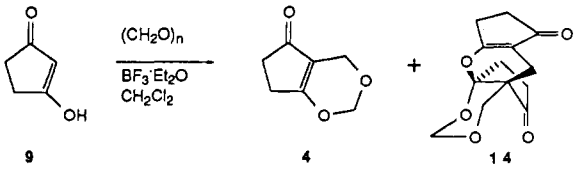


Table I. Preparation of 6,7-Dihydrocyclopenta-1,3-dioxin-5(4*H*)-one 4: Exploratory Studies



entry	9 mmol	$(CH_2O)_n$, equiv	BF_3·Et_2O, equiv	solv, mL	yield, % 4	yield, % 14
1	2	3	0.33	12	10	
2	2	5	1.2	12	11	
3	2	6.6	2.4	12	59	4
4	2	6.6	2.4	25	59	6
5	2	6.6	2.4	12[a]	13	
6	2	6	4	12	66	8
7	20	6	3	120	73	9

[a] CH_2Cl_2/Et_2O (1:1).

For our purposes, we required that formaldehyde or an equivalent thereof serve as the electrophile. Toward this end, treatment of a methylene chloride solution of 1,3-cyclopentanedione (**9**) and powdered paraformaldehyde (3 equiv) with BF_3·Et_2O (0.33 equiv) at ambient temperature, according to the Crow protocol, afforded a white crystalline solid (mp 72–73 °C). Structure **4** was assigned on the basis of its spectral properties (vide infra), in conjunction with its elemental composition data. The yield, however, was quite low (ca. 10%). To maximize the efficiency of the process, a systematic investigation was undertaken; the results are illustrated in Table I. The key to improving this reaction involved use of a larger excess of paraformaldehyde, as well as increasing the BF_3·Et_2O to paraformaldehyde ratio. Presumably the latter results in a more rapid breakdown of paraformaldehyde to formaldehyde and/or its BF_3·Et_2O complex, similar to the known ability of sulfuric acid to depolymerize paraformaldehyde.[7] Best results were obtained when 6 equiv of paraformaldehyde and 3 equiv of BF_3·Et_2O were employed; under these conditions, dioxin **4** was produced in 70–75% yield. Importantly, **4** was quite stable; it could be purified conveniently via silica gel chromatography without noticeable reaction with oxygen (vide supra).

In addition to vinylogous ester **4**, a small amount (ca. 10%) of a novel crystalline propellane (i.e., **14**) was also produced. The structure of the propellane, initially quite obscure on the basis of spectral data alone, was established through aegis of a single-crystal X-ray analysis.[8]

Having maximized the Prins reaction with 1,3-cyclopentanedione (**9**), we expanded our study to include the

(4) Smith, A. B., III In "Evolution of a Synthetic Strategy: Total Synthesis of (±)-Jatrophone" *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic: New York, 1984; Chapter 9, pp 224–254.

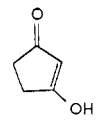
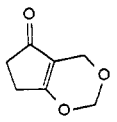
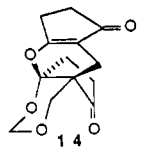
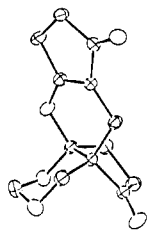
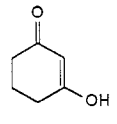
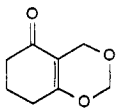
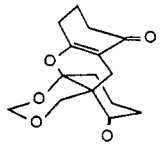
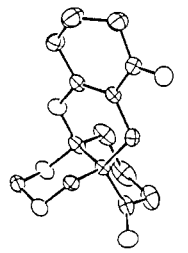
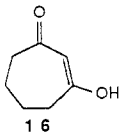
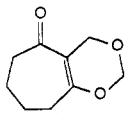
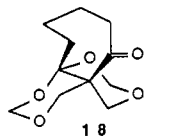
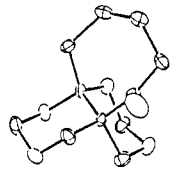
(5) Bolte, M. L.; Crow, W. D.; Yoshida, S. *Aust. J. Chem.* **1982**, *35*, 1411.

(6) For reviews on the Prins reaction, see: Adams, D. R.; Bhatnagar, S. P. *Synthesis* **1977**, 661. Arundale, E.; Mikeska, L. A. *Chem. Rev.* **1952**, *51*, 505.

(7) Tomoskozi, I.; Gruber, L.; Kovacs, G.; Szekely, I.; Simonidesz, V. *Tetrahedron Lett.* **1976**, 4639.

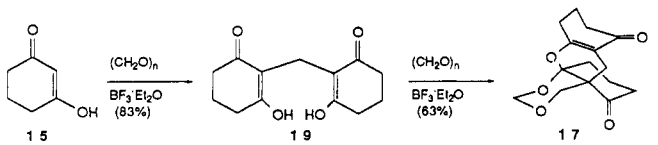
(8) Unpublished results of P. Carroll, University of Pennsylvania X-Ray Crystallographic Center.

Table II. Preparation of 1,3-Dioxin Vinylogus Esters

entry	substrate	conditions[a]	time, h	products and yields	
	 9			 4	 14 = 
1		A	38	73%	9%
2		B	30	78%	4%
	 15			 5	 17 = 
3		A	32	40%	9%
4		B	18	84%	16%
	 16			 6	 18 = 
5		A	2	72%	9%
6		B	5	49%	44%

[a] Conditions A: paraformaldehyde (6 equiv) and BF_3·Et_2O (3 equiv), 0.16 M in CH_2Cl_2, room temperature. Conditions B: trioxane (6 equiv) and BF_3·Et_2O (3 equiv), 0.02 M in CH_2Cl_2, room temperature.

six- and seven-membered 1,3-diketones **15** and **16**. As illustrated in Table II, application of the aforementioned conditions to 1,3-cyclohexanedione (**15**) led to the corresponding six-membered ring vinylogous ester **5**; the yield, however, was only 40% (Table II, Entry 3). Again, a small amount (9%) of what appeared to be an analogous propellane was obtained. X-ray crystal analysis confirmed structure **17**.[8] After considerable experimentation a substantial improvement in the yield of **5** was realized when trioxane was substituted for paraformaldehyde. Further progress (i.e., 84%) was achieved when a syringe pump was employed to add the 1,3-diketone to a mixture of trioxane and BF_3·Et_2O over a 2.5-h period, the total reaction period being 18 h (Table II, Entry 4). A modest improvement in yield (74–78%) was also noted in the case of 1,3-cyclopentanedione (**9**), when the trioxane–syringe pump protocol was employed (Table II, entry 2). Finally, when 1,3-cyclohexanedione (**15**) was subjected to the original Crow conditions[5] (i.e., 0.33 equiv of BF_3·Et_2O), a new product was obtained in 83% yield. The latter was shown by IR and high-field NMR in conjunction with elemental composition data to possess structure **19**. Subsequent treatment of **19** with excess paraformaldehyde (10 equiv) and BF_3·Et_2O (1.5 equiv) in methylene chloride led to propellane **17** in 63% yield. Interestingly, an intermediate analogous to **19** was not observed with 1,3-cyclopentanedione.



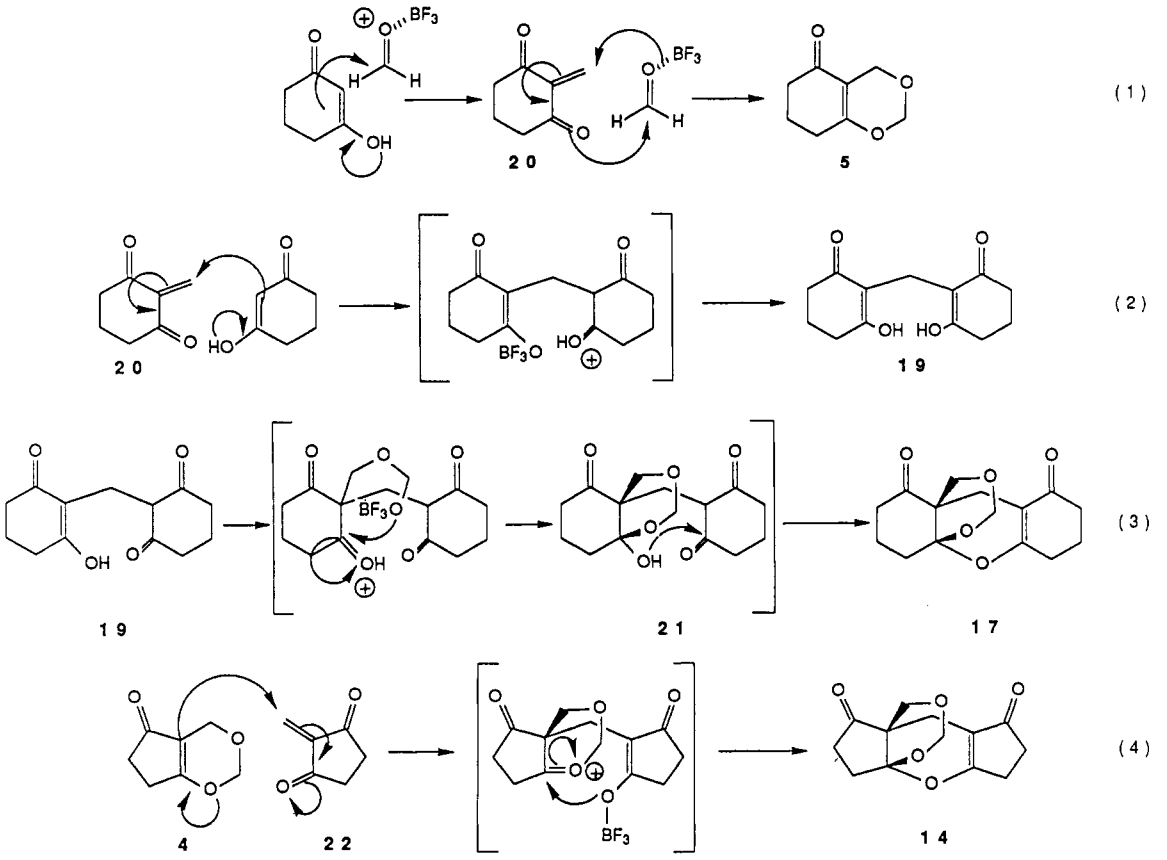
15 19 17

To account for the above product distribution, in particular formation of propellanes **14** and **17** as well as intermediate **19**, the following scenario is proposed (Scheme II). As in the Crow mechanism, the central intermediate is believed to be **20**, which reacts with a second equivalent of BF_3–formaldehyde complex to afford the 1,3-dioxin system (eq 1). If, however, the concentration of formaldehyde is low, as with the conditions originally developed by Crow, **20** is envisioned to undergo coupling with a second equivalent of 1,3-cyclohexanedione to afford **19** (eq 2). Alternatively, if the reaction is allowed to proceed, or if **19** is resubjected to the reaction conditions, a second Prins reaction with formaldehyde, followed by addition of a third equivalent of formaldehyde leads to **21** (eq 3). Ring closure to the tetracyclic skeleton, followed by loss of H_2O·BF_3 would then afford propellane **17**. To explain formation of propellane **14** in the case of 1,3-cyclopentanedione (**9**), wherein an intermediate corresponding to **19** was not observed, we suggest that dioxin **4** reacts with **22** as illustrated in eq 4.

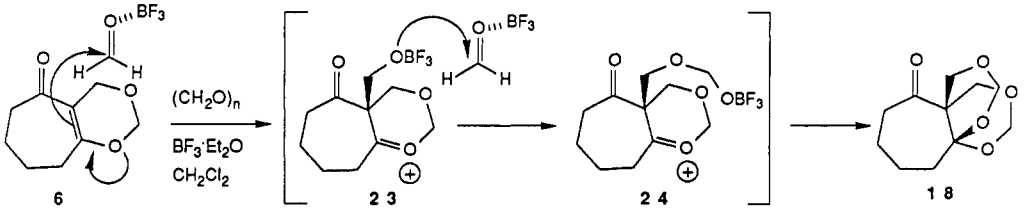
Turning next to 1,3-cycloheptanedione (**16**),[9] best results were obtained with paraformaldehyde and BF_3·Et_2O (Table II, entry 5). In this case vinylogous ester **6** was obtained in 72% yield, again along with a small amount of a crystalline propellane. Elemental composition data quickly indicated that this propellane was not a simple analogue of the previous two propellanes but instead involved condensation of 1,3-cycloheptanedione (**16**) with 4 equiv of formaldehyde. X-ray analysis revealed structure **18**.[8] In this case, it would appear as if vinylogous ester **6** undergoes a second Prins reaction and that the resultant

(9) Bhushan, V.; Chandrasekaran, S. *Synth. Commun.* **1984**, *14*, 339.

Scheme II



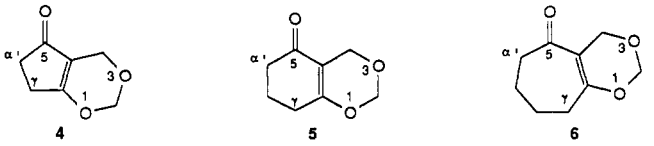
Scheme III



intermediate (**23**) reacts with an additional equivalent of formaldehyde (Scheme III).

Table III records the spectral data for the dioxin vinylogous esters **4**–**6**. The ^1H and ^{13}C NMR assignments were straightforward, based primarily on chemical shift expectations.[10] In particular, the C(2)-methylene protons resonate furthest downfield at δ 5.05–5.25 in the ^1H NMR spectra, while the C(4)-allylic methylene hydrogens appear at δ 4.40–4.50, possessing characteristic long-range allylic coupling to the γ-methylene protons. This long-range coupling proved particularly diagnostic vis-à-vis structure assignments during the course of our study on the alkylation of the vinylogous ester system (vide infra). Characteristic infrared absorptions were also readily discernable (Table III). In addition to strong bands at ca. 3000 cm^{-1} for the C–H stretching modes, carbonyl absorptions were observed at ca. 1620–1700 cm^{-1}, the particular frequency dependent upon ring size.[11] Finally, typical π to π^* electronic absorptions were observed in the ultraviolet spectra in the range of 235–260 nm (ϵ 10^3–10^4) due to the

Table III. Spectroscopic Properties of the 1,3-Dioxin Vinylogous Esters



	^1H NMR (250 MHz $CDCl_3$), δ			
compd	C(2)H_2	C(4)H_2	C(α')H_2	C(γ)H_2
4	5.25 (s)	4.48 (dd, J = 1.8 Hz)	2.63–2.68 (m)	2.40–2.44 (m)
5	5.14 (s)	4.44 (dd, J = 1.9 Hz)	2.35–2.46 (m)	2.35–2.46 (m)
6	5.06 (s)	4.41 (dd, J = 1.4 Hz)	2.55–2.62 (m)	2.55–2.62 (m)

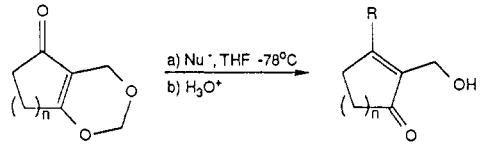
	^{13}C NMR (62.9 MHz $CDCl_3$), δ				
compd	C(2)	C(4)	C(4a)	C(5)	C(β)
4	92.4	62.7	114.4	200.8	181.8
5	91.1	62.4	111.3	195.8	169.9
6	90.8	63.9	114.0	199.2	170.6

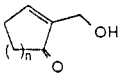
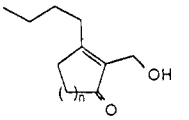
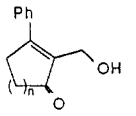
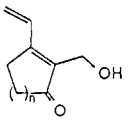
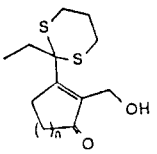
	IR ($CHCl_3$)	UV (EtOH)	
compd	ν_{max}, cm^{-1}	$\lambda_{max}(\pi-\pi^*)$, nm	ϵ_{max}
4	2995, 1700, 1640	235	17 500
5	3000, 1640, 1625	255	7800
6	3000, 1630, 1620	260	7200

(10) Jackman, L. M.; Sternell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; 2nd ed.; Pergamon: Oxford, 1969; Chapter 3, p 159.

(11) Nakanishi, K.; Solomon, P. H. *Infrared Absorption Spectroscopy*, 2nd ed.; Holden-Day: San Francisco, 1977; Chapter 4, p 66.

Table IV. Reductive and Alkylative 1,3-Carbonyl Transposition of 1,3-Dioxin Vinylogus Esters



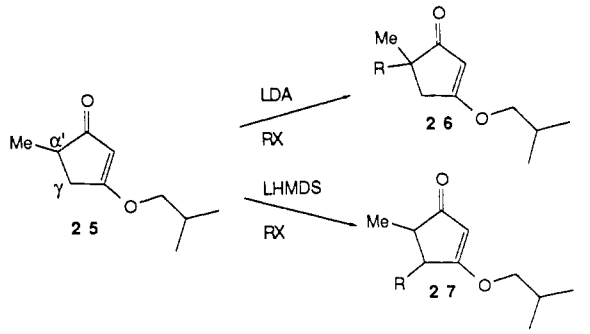
entry	nucleophile	n	yield, %	product
1	DIBAL	1	91	
2		2	91	
3		3	84	
4	$LiAlH_4$	1	81	
5	BuLi	1	95	
6		2	66	
7		3	89	
8	PhLi	1	78	
9		2	93	
10		3	87	
11		1	94	
12		2	76	
13		3	86	
14		1	81	
15		2	93	
16		3	74	

vinylogous ester chromophore.[12]

The Chemical Reactivity of the Dioxin Vinylogous Esters. Having successfully developed effective syntheses of dioxins **4–6**, we set out to explore their chemical reactivity. In view of our ongoing bertyadionol synthetic program and related efforts, we were particularly interested in two types of reactivity: (A) reductive and alkylative 1,3-carbonyl transpositions;[3] and (B) regioselective alkylation and hydroxylation with carbon and oxygen electrophiles respectively.[13] We anticipated that such transformations, if successful, would not only prove useful for our program but would greatly enhance the general utility of the dioxin vinylogous ester system for complex molecule synthesis.

(A) Reductive and Alkylative 1,3-Carbonyl Transpositions. Reductive and alkylative 1,3-carbonyl transpositions of vinylogous esters are well precedented.[3] To explore the feasibility of such processes with dioxins **4–6**, we selected a number of readily available nucleophiles. Our results are listed in Table IV. Several comments are in order. First, a variety of simple β-unsubstituted or β-substituted α-hydroxymethyl enones can be readily prepared in high yield in two operations from the corresponding 1,3-diketone. For simple α-hydroxymethyl enones both Dibal-H and $LiAlH_4$ were effective. The economy of this operation should be contrasted to the multistep procedures previously developed in our laboratory for the construction of even the simplest α-hydroxymethyl enone systems (e.g., 2-(hydroxymethyl)cyclopentenone and -cyclohexenone).[14] Second, entries 11–13 highlight a variety of dienes now readily available for possible use in Diels–Alder reactions. Third, acyl anion equivalents (see entries 14–16) provide access to latent 1,4-enedione units, the latter encountered in the structure of bertyadionol and related natural products. Finally it should be emphasized that the specific nucleophiles chosen for this study represent only a fraction of those that could be employed.

(B) Alkylation and Hydroxylation Reactions. Recently, Koreeda and co-workers[15] recorded the results of their investigation on the alkylation of a structurally related vinylogous ester, 3-isobutoxycyclopent-2-en-1-ones (**25**). They noted that alkylation could be effected at either the α' or γ-position, depending on the amide base employed. For example, when lithium diisopropylamide was used, kinetic deprotonation at the α'-carbon resulted, while lithium bis(trimethylsilyl)amide led to the extended γ-enolate. In both cases the alkylation process proceeded regioselectively to afford either **26** or **27**.

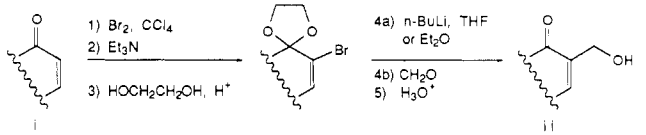


In light of these observations, we examined the alkylation and hydroxylation of the enolates derived from vinylogous esters **4–6**, employing a variety of amide bases. As electrophiles we selected methyl iodide and the Davis oxaziridines.[16] Our results are outlined in Table V; yields, although not maximized, were good. Best results were obtained with THF as solvent. Importantly, the regiochemical outcome was found to depend both on the choice of amide base and the substitution pattern of the vinylogous ester. For example, treatment of **4–6** with 1.1 equiv of LDA in THF led to the presumed kinetic enolate [i.e., α'], which upon treatment with either methyl iodide or the Davis oxaziridines afforded the corresponding α'-derivative as the major products. In the case of **4** only, small amounts

(12) Scott, A. I. *Interpretation of Ultraviolet Spectra of Natural Products*; Pergamon: Oxford, 1964; Chapter 2, p 45.

(13) For leading references, see: Evans, D. A. In "Stereoselective Alkylation Reactions of Chiral Metal Enolates" *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Chapter 1, p 1.

(14) We refer here to the α-ketovinyl anion methodology developed in our laboratory for the conversion of cyclic enones (i.e., i) to the corresponding α-hydroxymethyl system (ii). In the case of cyclopentenone

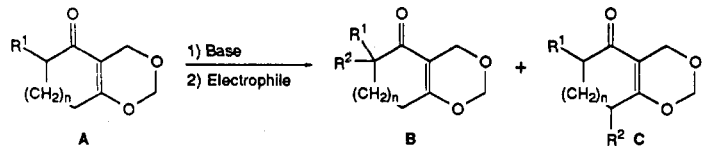


the overall yield for the five steps is 65%. For leading references, see: Guaciaro, M. A.; Wovkulich, P. M.; Smith, A. B., III. *Tetrahedron Lett.* **1978**, 4661. Smith, A. B., III; Branca, S. J.; Pilla, N. P.; Guaciaro, M. A. *J. Org. Chem.* **1982**, *47*, 1855. Smith, A. B., III; Branca, S. J.; Guaciaro, M. A.; Wovkulich, P. A.; Korn, A. *Org. Synth.* **1983**, *61*, 65.

(15) Koreeda, M.; Liang, Y.; Akagi, H. *J. Chem. Soc., Chem. Commun.* **1979**, 449. Koreeda, M.; Mislankar, S. G. *J. Am. Chem. Soc.* **1983**, *105*, 7203. Koreeda, M.; Liang Chen, Y. P. *Tetrahedron Lett.* **1981**, *22*, 15.

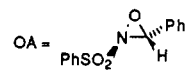
(16) For leading references on the oxygen-transfer reactions of 2-sulfonyloxaziridines, see the following. (a) Alkenes: Davis, F. A.; Abdul-Malik, N. F.; Awad, S. B.; Harakal, M. E. *Tetrahedron Lett.* **1981**, *22*, 917. Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123. (b) Sulfides/disulfides: Davis, F. A.; Jenkins, R. H., Jr.; Yocklovich, S. G. *Tetrahedron Lett.* **1978**, 5171. Davis, F. A.; McCauley, J. P., Jr.; Harakal, M. E. *J. Org. Chem.* **1984**, *49*, 1465. (c) Selenides: Davis, F. A.; Stringer, O. D.; Billmers, J. M. *Tetrahedron Lett.* **1983**, *24*, 1213.

Table V. Alkylation and Hydroxylation of Vinylogous Esters 4–6

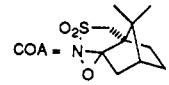


entry	n	R^1	base[b]	solv	electrophile	product, R^2	yield, % B	yield, % C
1	0	H	LDA	THF	MeI	Me	61	3
2	0	H	LiHMDS	THF	MeI	Me	53	<5
3	0	H	LDA	DME	OA	OH	33[a]	6[a]
4	0	H	NaHMDS	THF	OA	OH	35[a]	36[a]
5	0	Me	LDA	THF	OA	OH	51	0
6	0	Me	LDA	DME	OA	OH	57	0
7	0	Me	NaHMDS	THF	OA	OH	4	76
8	0	H	LDA	THF	COA	OH	45[a]	4[a]
9	0	Me	LDA	THF	COA	OH	68	4
10	0	Me	NaHMDS	THF	COA	OH	3	28
11	1	H	LDA	THF	MeI	Me	78	0
12	1	H	LDA	DME	OA	OH	58	0
13	1	H	NaHMDS	THF	OA	OH	49	37
14	2	H	LDA	THF	MeI	Me	73	0
15	2	H	LDA	DME	OA	OH	54	0
16	2	H	NaHMDS	THF	OA	OH	51	37

[a] Based on recovered starting materials. [b]



(±)-28



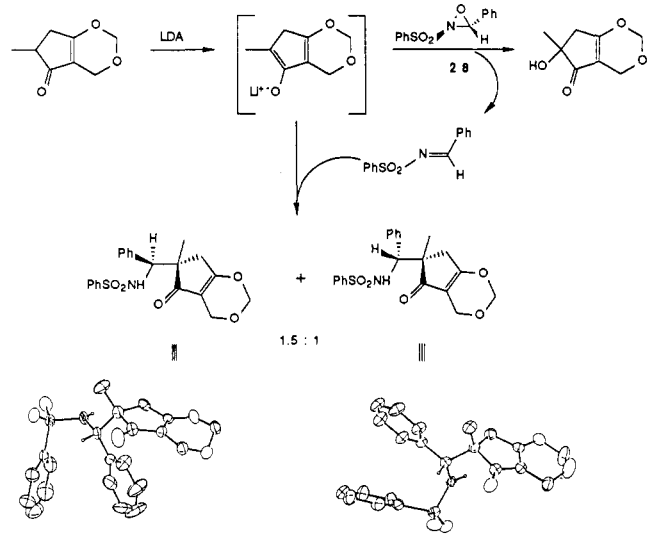
(+)(2R, 8aS)-29

(3–5%) of both γ-monomethylated and α′,γ-dimethylated products were obtained. Surprisingly, lithium bis(trimethylsilyl)amide resulted in essentially the same α′:γ ratio (entry 2). On the other hand, use of sodium bis(trimethylsilyl)amide led to a significant increase in γ-alkylation. High γ-selectivity however was only observed when the α′-position was substituted; entry 7 (R^1 = Me, n = 0) best illustrates this point.

In several cases (entries 5, 6, 12, and 15), the hydroxylations were complicated by a side reaction which involved addition of the vinylogous ester enolate to the sulfonimine derived from 2-(phenylsulfonyl)-3-phenyloxaziridine (**28**), to afford a diastereomeric mixture (ca. 1:1) of imino aldol products (Scheme IV).[17] In each case these products were fully characterized. Their structures were assigned on the bases of spectral and elemental composition data, and in one example (entry 6) the assigned structures of both diastereomers were confirmed by single-crystal X-ray analyses. Fortunately, this minor complication can be conveniently circumvented through use of the (camphorylsulfonyl)oxaziridine **29**, which, as Davis[18] noted, does not give rise to imino aldol side products in enolate hydroxylations (entries 8–10). Finally, only low levels (ca. 16% ee) of asymmetric induction were observed with this homochiral reagent.

The structures of the alkylated and hydroxylated products were initially assigned on the basis of their ^{1}H NMR spectra. As alluded to above, the coupling pattern observed for the C(4)-methylene protons proved to be particularly diagnostic of the regiochemical outcome. In the case of α′-substitution, a characteristic long-range

Scheme IV



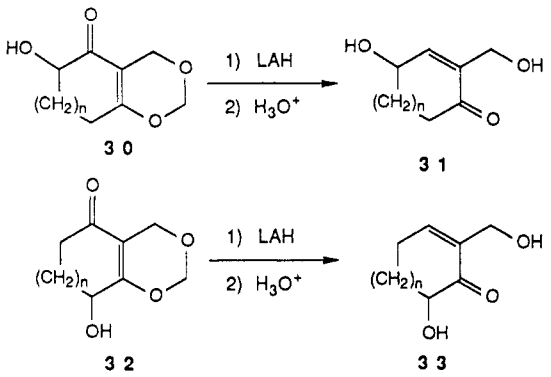
ABXY multiplet (i.e., ddd) resulted, wherein the C(4)-methylene protons were clearly magnetically nonequivalent. Monosubstitution at the γ-position, on the other hand, led to an ABX pattern (i.e., dd) for both C(4)-methylene protons. In this case the C(4)-methylene protons appeared more nearly magnetically equivalent, thereby greatly simplifying the observed coupling pattern, which in some cases appeared as an apparent doublet.

To confirm the above structural assignments, the α′- and γ-products in several cases were individually subjected to reductive 1,3-carbonyl transposition to afford the corresponding α-hydroxymethyl α,β-enone. Regiochemical differentiation was possible via NMR proton–proton decoupling experiments.[10] For example, when the C(4)-hydroxyl methine proton in **31** (n = 2) (easily assigned on the basis of the chemical shift) was irradiated, the doublet at δ 6.70 (J = 2.0 Hz) due to the vicinal olefinic proton

(17) Davis, F. A.; Haque, M. S.; Ulatowski, T. G.; Towson, J. C. *J. Org. Chem.* **1986**, *51*, 2402. Davis, F. A.; Vishwakarma, L. C. *Tetrahedron Lett.* **1985**, *26*, 3539. Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346.

(18) Davis, F. A.; Haque, M. S. *J. Org. Chem.* **1986**, *51*, 4083. Davis, F. A.; Wei, J.; Sheppard, A. C.; Guberwick, S. *Tetrahedron Lett.* **1987**, *28*, 5115. Davis, F. A.; Ulatowski, T. G.; Haque, M. S. *J. Org. Chem.* **1987**, *52*, 5288. Davis, F. A., Drexel University, private communication.

collapsed to a singlet. In the case of γ-product **32** (n = 2), no change occurred in the corresponding vinyl resonance of **33** (n = 2), upon irradiation of the hydroxyl methine proton, but rather a simplification occured in the upfield aliphatic pattern.



Summary

An efficient, general preparation of simple 1,3-dioxin vinylogous esters has been achieved. Their potential as effective β-ketovinyl cation equivalents has been demonstrated via a variety of reductive and alkylative 1,3-carbonyl transpositions. Finally, regioselective alkylation and hydroxylation at the α′-position (and in some cases at the γ-position) further attests to the potential that the 1,3-dioxin vinylogous ester system holds in organic synthesis.

Experimental Section

Materials and Methods. Reactions were carried out under an argon atmosphere, using dry freshly distilled solvents, under anhydrous conditions in vacuum-flamed glassware, unless otherwise noted. Diethyl ether, DME, and THF were distilled under nitrogen from sodium/benzophenone, while benzene and dichloromethane were distilled from calcium hydride. Diisopropylamine, hexamethyldisilylamine, triethylamine, and pyridine were distilled from calcium hydride and stored over KOH. n-butyllithium and sodium bis(trimethylsilyl)amide were purchased from Aldrich and standardized by titration with diphenylacetic acid. Solutions were dried over $MgSO_4$.

All reactions were monitored by thin-layer chromatography (TLC) using 0.25-mm E. Merck precoated silica gel plates. Flash column chromatography was performed with the solvents indicated using silica gel-60 (particle size 0.040–0.063 mm) supplied by E. Merck. The purity of the products on which yields are reported was determined to be ≥95% on the basis of ^1H NMR spectral and/or chromatographic analyses, unless stated otherwise.

All melting points are corrected. Proton NMR were recorded at 250 or 500 MHz. Carbon-13 NMR spectra were obtained at 69.5 MHz.

The single-crystal X-ray structures were determined by Dr. Patrick Carroll of the University of Pennsylvania with a CAD-4 automated diffractometer.

6,7-Dihydrocyclopenta-1,3-dioxin-5(4*H*)-one (4). A mixture of 1,3-cyclopentanedione (3.24 g, 33.0 mmol), paraformaldehyde (6.00 g, 200 mmol), BF_3·Et_2O (12.6 mL, 100 mmol) and methylene chloride (200 mL) was stirred vigorously at room temperature for 38 h. The mixture was then filtered and the filtrate added to 10% NaOH (130 mL) and ice (50 g). The resultant aqueous layer was extracted with methylene chloride (3 × 75 mL), and the combined organic phases were washed with brine and dried over $MgSO_4$. Removal of the solvent in vacuo and purification of the residue via flash column chromatography (silica; hexane/acetone, 3:1) afforded two compounds.

The first product to elute was vinylogous ester **4**: 3.36 g (73%, as a white solid), which was recrystallized from hexane/EtOAc (5:1) to afford an analytically pure sample (mp 73–75 °C); UV (EtOH) λ_{max} 234 nm (ε 17 500); IR ($CHCl_3$) 3000 (m), 1690 (m), 1640 (s), 1430 (m), 1310 (m), 1205 (m), 1180 (m), 1090 (br m), 910 (s), 890 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.41–2.52 (m, 2 H), 2.60–2.71 (m, 2 H), 4.49 (t, J = 2.1 Hz, 2 H), 5.24 (s 2 H); ^{13}C NMR (69.5 MHz, $CDCl_3$) δ 26.2, 32.3, 62.7, 92.4, 114.4, 181.8, 200.8; mass spectrum, m/e 140.0482 (M^+ calcd for $C_7H_8O_3$, 140.0473).

Anal. Calcd for $C_7H_8O_3$: C, 60.00; H, 5.75. Found: C, 60.19; H, 5.82.

The second product to elute was propellane **14**: 0.359 g (9%) of a colorless solid, which was recrystallized from hexane/EtOAc to afford an analytically pure sample (mp 178–180 °C) suitable for X-ray analysis; IR ($CHCl_3$) 3000 (m), 1760 (s), 1700 (m), 1650 (s), 1450 (m), 1400 (s), 1195 (m), 1165 (m), 970 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.95–2.11 (m, 3 H), 2.35–2.45 (m, 1 H), 2.50–2.75 (m, 6 H), 3.32 (d, J = 11.7 Hz, 1 H), 4.24 (d, J = 11.7 Hz, 1 H), 4.83 (d, J = 6.4 Hz, 1 H), 4.88 (d, J = 6.6 Hz, 1 H); mass spectrum, m/e 250.0836 (M^+ calcd for $C_{13}H_{14}O_5$, 250.0841).

Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.47; H, 5.63.

4,6,7,8-Tetrahydro-5*H*-1,3-benzodioxin-5-one (5). Method A. A mixture of 1,3-cyclohexanedione (0.224 g, 1.940 mmol), paraformaldehyde (0.360 g, 12.00 mmol), BF_3·Et_2O (0.738 mL, 6.00 mmol) and methylene chloride (12.5 mL) was stirred at room temperature for 38 h. The reaction mixture was then quenched with saturated $NaHCO_3$ (20 mL) and the aqueous phase extracted with methylene chloride (3 × 20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to afford a yellow oil. Purification via flash column chromatography (gradient elution, hexanes/EtOAc, 4:1 to 3:1) afforded two compounds.

The first compound to elute was vinylogous ester **5**: 0.1173 g (40%) of a colorless oil; UV (EtOH) λ_{max} 255 nm (ε 7800); IR ($CHCl_3$) 3000 (m), 2950 (m), 2870 (m), 1630 (br s), 1415 (s), 1395 (s), 950 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.96–2.06 (m, 4 H), 2.35–2.46 (m, 2 H), 4.44 (dd, J = 2.0, 1.9 Hz, 2 H), 5.14 (s, 2 H); mass spectrum, m/e 155.0708 (MH^+ calcd for $C_8H_{11}O_3$, 155.0708).

The second compound to elute was propellane **17**: 0.0448 g (9%) of a white solid; recrystallization from hexane/EtOAc gave an analytically pure sample (mp 142–144 °C) suitable for X-ray analysis; IR ($CHCl_3$) 3000 (m), 2950 (m), 2880 (m), 1715 (s), 1630 (s), 1385 (s), 1185 (s), 1160 (s), 930 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.85–2.09 (m, 7 H), 2.35–2.60 (m, 7 H), 3.32 (d, J = 11.4 Hz, 1 H), 4.43 (d, J = 11.4 Hz, 1 H), 4.85 (d, J = 5.9 Hz, 1 H), 5.06 (d, J = 5.9 Hz, 1 H); mass spectrum, m/e 279.1232 (MH^+ calcd for $C_{15}H_{19}O_5$, 279.1232).

Method B. To a solution of trioxane (1.080 g, 12.00 mmol), BF_3·Et_2O (0.738 mL, 6.00 mmol) and methylene chloride (100 mL) was added a solution of 1,3-cyclohexanedione (0.230 g, 2.00 mmol) dissolved in 2 mL of methylene chloride over a period of 2.5 h at room temperature. The resultant mixture was allowed to stir for an additional 16 h, after which time saturated $NaHCO_3$ (40 mL) was added. The aqueuos layer was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic phases were washed with brine, dried, and concentrated in vacuo. Flash column chromatography (gradient elution; hexanes/EtOAc, 4:1 to 3:1) afforded 0.260 g (84%) of the vinylogous ester **5** together with 0.101 g (16%) of the propellane **17**.

Intermediate 19. A solution of 1,3-cyclohexanedione (0.250 g, 1.785 mmol), paraformaldehyde (0.160 g, 5.330 mmol), BF_3·Et_2O (0.073 mL, 0.590 mmol), and methylene chloride (8 mL) was stirred at room temperature. After 2 h saturated $NaHCO_3$ (10 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were washed with brine (1 × 10 mL), dried over $MgSO_4$, and concentrated in vacuo. Purification via flash column chromatography (hexanes/acetone, 4:1) yielded 0.278 g (83%) of a white solid, which was recrystallized from EtOAc/hexanes to afford an analytically pure sample (mp 134–135 °C): IR ($CHCl_3$) 3300–2100 (br, s), 3000 (m), 2965 (s), 2880 (m), 1605 (br s), 1585 (br s), 1385 (s), 1265 (s), 900 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.85–1.98 (m, 4 H), 2.27–2.53 (m, 8 H), 3.13 (s, 2 H), 11.98 (br s 2 H); mass spectrum, m/e 236.1036 (M^+ calcd for $C_{13}H_{16}O_4$, 236.1048).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.82. Found: C, 66.33, H, 6.77.

Conversion of Intermediate 19 to Propellane 17. A solution of **19** (0.0585 g, 0.247 mmol), paraformaldehyde (0.074 g, 2.478

mmol), BF_3·Et_2O (0.036 mL, 0.297 mmol), and CH_2Cl_2 (2 mL) was stirred at room temperature. The reaction mixture was quenched with saturated $NaHCO_3$ (10 mL), and after 24 h the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Flash column chromatography (hexane/EtOAc, 2:1) afforded 0.0412 g (63%) of propellane **17**.

6,7,8,9-Tetrahydrocyclohepta-1,3-dioxin-5(4*H*)-one(6). A solution of 1,3-cycloheptanedione (0.0634 g, 0.5031 mmol), paraformaldehyde (0.0905 g, 3.019 mmol), BF_3·Et_2O (0.185 mL, 1.509 mmol), and CH_2Cl_2 (3.5 mL) was stirred at room temperature for 3 h. Saturated $NaHCO_3$ (10 mL) was then added, the aqueous phase extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic phases were washed with brine, dried, and concentrated in vacuo to give a yellow oil. Flash column chromatography (gradient elution, hexanes/EtOAc, 9:1 to 6:1) afforded two products.

The first product to elute was propellane **18**: 0.0104 g (9%, of a white solid), which was recrystallized from hexane/EtOAc to afford an analytical sample (mp 110–111 °C) suitable for X-ray analysis; TLC, R_f 0.46 (hexanes/EtOAc, 3:1); IR ($CHCl_3$) 3000 (m), 2925 (m), 2860 (s), 1685 (s), 1180 (s), 1035 (s), 945 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.62–2.11 (m, 6 H), 1.90–2.08 (br s, 2 H), 1.74 (d, J = 10.2 Hz, 2 H), 4.05–4.11 (m, 2 H), 4.94 (d, J = 6.2 Hz, 2 H), 5.22 (br d, J = 5.8 Hz, 2 H); mass spectrum, m/e 229.1054 (MH^+ calcd for $C_{11}H_{17}O_5$, 229.1076).

Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.87; H, 7.07. Found: C, 57.96; H, 7.08.

The second product to elute was vinylogous ester **6**: 0.0604 g (72%) of a colorless oil; TLC, R_f 0.30 (hexanes/EtOAc, 3:1); UV (EtOH) λ_{max} 260 nm (ε 7200); IR ($CHCl_3$) 3000 (m), 2940 (s), 2870 (s), 1620 (br s), 1390 (s), 1245 (s), 985 (s), 905 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.78–1.90 (m, 4 H), 2.55–2.62 (m, 4 H), 4.41 (dd, J = 1.4, 1.3 Hz, 2 H), 5.06 (s, 2 H); mass spectrum, m/e 169.0884 (MH^+ calcd for $C_9H_{13}O_3$, 169.0864).

General Procedure for Dibal 1,3-Ketone Transpositions: Preparation of 2-(Hydroxymethyl)-2-cyclopentenone. Dibal (1.0 M in hexanes, 0.60 mL, 0.60 mmol) was added dropwise to a cold solution (−78 °C) of the vinylogous ester **4** (0.070 g, 0.50 mmol) dissolved in 2 mL of THF. The resultant mixture was stirred for 2 h at −78 °C, and then MeOH (0.05 mL) and saturated aqueous Rochelle salt (1 mL) were added. After the mixture was stirred for 30 min at room temperature the aqueous layer was extracted with methylene chloride (3 × 5 mL), and the resultant organic phases were evaporated in vacuo to give a yellow oil, which was in turn dissolved in THF (3 mL) and treated with 5% HCl (0.05 mL). After 5 min, K_2CO_3 (0.050 g) was added, followed by 30 mL of ether. The resultant solution was dried over $MgSO_4$ and then concentrated in vacuo. Flash chromatography (hexanes/EtOAc, 1:2) of the residue yielded 0.051 g (91%) of a colorless solid (mp 68–69 °C), identical in all respects with an authentic sample.[18]

2-(Hydroxymethyl)-2-cyclohexenone: Dibal; colorless oil (91%); TLC, R_f 0.28 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3620–3260 (br m), 2995 (m), 2920 (m), 1665 (s), 1370 (s), 1005 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.96–2.07 (m, 2 H), 2.37–2.48 (m, 4 H), 2.89 (br s, 1 H), 4.25 (br s, 2 H), 6.96 (dd, J = 4.2, 4.1 Hz, 1 H); mass spectrum, m/e 127.0749 (MH^+ calcd for $C_7H_{11}O_2$, 127.0759).

2-(Hydroxymethyl)-2-cycloheptenone: Dibal; colorless oil (84%); flash column chromatography (hexanes/EtOAc, 1:1); TLC, R_f 0.18 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3680–3180 (br s), 3000 (s), 2925 (s), 2860 (s), 1650 (s), 1450 (s), 1385 (s), 1000 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.76–1.83 (m, 4 H), 2.42–2.50 (m, 2 H), 2.60–2.66 (m, 2 H), 2.91 (br s, 1 H), 4.22 (d, J = 3.0 Hz, 2 H), 6.76 (ddd, J = 6.2, 5.3, 0.9 Hz, 1 H); mass spectrum, m/e 140.0831 (M^+ calcd for $C_8H_{12}O_2$ 140.0837).

General Procedure for Alkylative 1,3-Ketone Transpositions. A solution of the vinylogous ester (0.360 mmol) dissolved in THF (1 mL, 0.12 M) was cooled to −78 °C for 10 min, and then the requisite lithium reagent (2 equiv) was added dropwise over a 5-min period. The reaction mixture was stirred for an additional 15 min and then quenched with 10% aqueous HCl (5 mL). After 20 min, the aqueous layer was extracted with ether (3 × 20 mL), and the combined organic phases were washed with brine (1 × 15 mL), dried over $MgSO_4$, and concentrated in vacuo to give the product, which was purified as indicated.

2-(Hydroxymethyl)-3-*n*-butyl-2-cyclopentenone: vinylogous ester **4** and *n*-BuLi; colorless oil (95%); flash column chromatography (hexanes/EtOAc, 1:1); TLC, R_f 0.25 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3600–3250 (br w), 3000 (m), 2970 (s), 2920 (s), 2855 (m), 1685 (s), 1635 (s), 1000 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.94 (t, J = 7.2 Hz, 3 H), 1.34–1.41 (m, 2 H), 1.50–1.59 (m, 2 H), 2.39–2.44 (m, 4 H), 2.50–2.60 (m 2 H), 3.81–4.04 (br s, 1 H), 4.34 (s, 2 H); mass spectrum, m/e 186.1488 ($M + NH_4^+$ calcd for $C_{10}H_{20}NO_2$, 186.1494).

2-(Hydroxymethyl)-3-*n*-butyl-2-cyclohexenone: vinylogous ester **5** and *n*-BuLi; colorless oil (66%); flash column chromatography (hexanes/EtOAc, 4:1); TLC, R_f 0.36 (hexanes/EtOAc, 3:1); IR ($CHCl_3$) 3600–3280 (br m), 3000 (s), 2960 (s), 2925 (s), 2860 (s), 1650 (s), 1620 (s), 1365 (s), 1180 (m), 1000 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3 H), 1.31–1.53 (m, 4 H), 1.86–2.01 (m, 2 H), 2.32 (dd, J = 8.1, 7.2 Hz, 2 H), 2.38–2.44 (m, 4 H), 2.91 (br s, 1 H), 4.34 (br s, 2 H); mass spectrum, m/e 183.1359 (MH^+ calcd for $C_{11}H_{19}O_2$, 183.1385).

2-(Hydroxymethyl)-3-*n*-butyl-2-cycloheptenone: vinylogous ester **6** and *n*-BuLi; colorless oil (89%); flash column chromatography (gradient elution; hexane/EtOAc, 4:1 to 3.1); TLC, R_f 0.16 (hexanes/EtOAc, 3:1); IR ($CHCl_3$) 3620–3280 (br w), 3015 (s), 2955 (s), 2880 (s), 1645 (br s), 1625 (br s), 1460 (m), 1000 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.93 (t, J = 7.1 Hz, 3 H), 1.34–1.49 (m, 4 H), 1.73–1.78 (m, 4 H) 2.32 (dd, J = 7.1, 7.1 Hz, 2 H), 2.43 (dd, J = 6.5, 6.2 Hz, 2 H), 2.56 (dd, J = 6.2, 4.8 Hz, 2 H), 2.90 (br s, 1 H), 4.29 (d, J = 4.4 Hz, 2 H); mass spectrum, m/e 197.1555 (MH^+ calcd for $C_{12}H_{21}O_2$, 197.1542).

2-(Hydroxymethyl)-3-phenyl-2-cyclopentenone: vinylogous ester **4** and PhLi; solid (78%) recrystallized from hexane/EtOAc (mp 86–87 °C); flash column chromatography (hexanes/EtOAc, 1:1); TLC, R_f 0.27 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3610–3200 (br m), 3000 (m), 2920 (m), 1685 (s), 1620 (s), 1450 (m), 1355 (s), 1000 (s), 695 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.56–2.60 (m, 2 H), 2.99 (dd, J = 5.4, 4.7 Hz, 2 H), 3.34 (t, J = 5.6 Hz, 1 H), 4.48 (d, J = 5.1 Hz, 2 H), 7.45–7.56 (m, 5 H); mass spectrum, m/e 188.0831, (M^+ calcd for $C_{12}H_{12}O_2$, 188.0837).

2-(Hydroxymethyl)-3-phenyl-2-cyclohexenone: vinylogous ester **5** and PhLi; solid (93%) recrystallized from hexane/EtOAc (mp 73–74 °C); flash column chromatography (hexanes/EtOAc, 1:1); TLC, R_f 0.34 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3620–3300 (br w), 3000 (m), 1655 (s), 1610 (w), 1360 (m), 1000 (m), 690 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.06–2.14 (m, 2 H), 2.53 (dd, J = 7.1, 6.3 Hz, 2 H), 2.69 (dd, J = 6.0, 6.0 Hz, 2 H), 2.90 (br s, 1 H), 4.19 (s, 2 H), 7.25–7.28 (m, 2 H), 7.34–7.41 (m, 3 H); mass spectrum, m/e 202.0976 (M^+ calcd for $C_{13}H_{14}O_2$, 202.0994).

2-(Hydroxymethyl)-3-phenyl-2-cycloheptenone: vinylogous ester **6** and PhLi; colorless oil (87%); flash column chromatography (hexanes/EtOAc, 3:1); TLC, R_f 0.15 (hexanes/EtOAc, 3:1); IR ($CHCl_3$) 3640–3200 (br m), 3000 (s), 2940 (s), 2865 (m), 1650 (s), 1600 (m), 1335 (m), 1000 (s), 700 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.86–2.91 (m, 4 H), 2.66–2.75 (m, 4 H), 2.99 (br t, J = 5.9 Hz, 1 H), 4.11 (d, J = 5.4 Hz, 2 H), 7.22–7.32 (m, 2 H), 7.34–7.41 (m, 3 H); mass spectrum, m/e 217.1228 (MH^+ calcd for $C_{14}H_{17}O_2$, 217.1229).

2-(Hydroxymethyl)-3-vinyl-2-cyclopentenone: vinylogous ester **4** and vinyllithium; colorless oil (94%); flash column chromatograpy (hexanes/EtOAc, 1:1); TLC, R_f 0.19 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3600–3250 (br w), 3000 (m), 2920 (m), 2850 (m), 1685 (s), 1635 (s), 1585 (m), 1360 (m), 1000 (s), 935 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.46–2.50 (m, 2 H), 2.72–2.76 (m, 2 H), 3.01 (br s, 1 H), 4.44 (d, J = 2.2 Hz, 2 H), 5.62 (d, J = 10.7 Hz, 1 H), 5.84 (d, J = 17.4 Hz, 1 H), 6.99 (dd, J = 17.5, 10.7 Hz, 1 H); mass spectrum, m/e 139.0751 (MH^+ calcd for $C_8H_{11}O_2$, 139.0759).

2-(Hydroxymethyl)-3-vinyl-2-cyclohexenone: vinylogous ester **5** and vinyllithium; colorless oil (76%); flash column chromatography (hexanes/EtOAc, 1:1): TLC, R_f 0.30 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3650–3250 (br w), 3000 (m), 2940 (m), 2880 (m), 1650 (s), 1620 (s), 1575 (m), 1370 (m), 1185 (m), 995 (s), 930 (m), cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.97–2.07 (m, 2 H), 2.47 (dd, J = 7.1, 6.3 Hz, 2 H), 2.57 (dd, J = 6.1, 6.1 Hz, 2 H), 2.81 (dd, J = 17.4, 0.6 Hz, 1 H), 4.47 (d, J = 6.2 Hz, 2 H), 5.57 (d, J = 11.0 Hz, 1 H), 5.75 (dd, J = 17.4, 0.6 Hz, 1 H), 6.99 (dd, J = 17.4, 11.0 Hz, 1 H); mass spectrum, m/e 152.0837 (M^+ calcd for $C_9H_{12}O_2$, 152.0837).

2-(Hydroxymethyl)-3-vinyl-2-cycloheptenone: vinylogous ester **6** and vinyllithium; colorless oil (86%); flash column chromatography (hexanes/EtOAc, 3:1); TLC, R_f 0.44 (hexanes/EtOAc, 1:1); IR ($CHCl_3$) 3600–3400 (br m), 3000 (m), 2960 (m), 2860 (m), 1645 (s), 1615 (m), 1570 (m), 990 (s), 920 (m), cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.72–1.82 (m, 4 H), 2.54–2.60 (m, 4 H), 2.88 (t, J = 6.2 Hz, 1 H), 4.40 (d, J = 6.0 Hz, 2 H), 5.48 (dd, J = 10.6, 0.4 Hz, 1 H), 5.69 (d, J = 17.2 Hz, 1 H), 6.94 (dd, J = 17.3, 11.0 Hz, 1 H); mass spectrum, m/e 166.1010 (M^+ calcd for $C_{10}H_{14}O_2$, 166.0994).

General Procedure for Addition of 2-Lithio-2-alkyldithianes: 2-(Hydroxymethyl)-3-(2-ethyl-1,3-dithian-2-yl)-2-cyclohexenone. A solution of 2-lithio-2-ethyl-1,3-dithiane (2.91 mL, 6.756 mmol) was generated at −20 °C by the addition of *n*-butyllithium to a solution of 2-ethyl-1,3-dithiane (1.00 g, 6.756 mmol) dissolved in 2.84 mL of THF. After 2 h at −20 °C, 636 μL (0.636 mmol) of this solution was added to a cold (−78 °C) solution of vinylogous ester **5** (0.049 g, 0.318 mmol) dissolved in 1 mL of THF. The reaction mixture was stirred for 5 min, and then 5 mL of 10% aqueous HCl was added and the stirring continued for 30 min. The resultant aqueous layer was extracted with ether (5 × 20 mL), and the combined organic phases were washed with saturated $NaHCO_3$ (1 × 5 mL) and brine (1 × 5 mL), dried, and concentrated in vacuo to afford a yellow oil, which was purified by flash column chromatography (gradient elution, hexanes/EtOAc, 3:1 to 2.5:1) to give 0.0802 g (93%) of a colorless oil: TLC, R_f 0.09 (hexanes/EtOAc, 3:1); IR ($CHCl_3$) 3600–3400 (br m), 3000 (m), 2970 (s), 1655 (s), 1580 (m), 1345 (m), 1080 (m), 1000 (s), 990 (s), cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.03 (t, J = 7.4 Hz, 3 H), 1.89–2.04 (m, 4 H), 2.27 (q, J = 7.4 Hz, 2 H), 2.43 (dd, J = 7.1, 6.4 Hz, 2 H), 2.75–2.86 (m, 5 H), 2.92–3.02 (m, 2 H), 4.80 (d, J = 6.1 Hz, 2 H); mass spectrum, m/e 273.0934 (MH^+ calcd for $C_{13}H_{21}O_2S_2$, 273.0983).

2-(Hydroxymethyl)-3-(2-ethyl-1,3-dithian-2-yl)-2-cyclopentenone: vinylogous ester **4** and 2-lithio-2-ethyl-1,3-dithiane; colorless oil (81%); flash column chromatography (hexanes/acetone, 3:1): IR ($CHCl_3$) 3500 (br s), 2995 (s), 2920 (s), 1690 (s), 1600 (m), 1430 (s), 1310 (s), 1250 (br m), 1005 (s), 990 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.93 (t, J = 7.4 Hz, 3 H), 1.95 (m, 2 H), 2.05 (q, J = 7.4 Hz, 2 H), 2.40 (m, 2 H), 2.65–2.80 (m, 6 H), 3.30 (br s, 1 H), 4.65 (s, 2 H); mass spectrum, m/e 258.0732 (M^+ calcd for $C_{12}H_{18}O_2S_2$, 258.0748).

2-(Hydroxymethyl)-3-(2-ethyl-1,3-dithian-2-yl)-2-cycloheptenone: vinylogous ester **6** and 2-lithio-2-ethyl-1,3-dithiane; colorless oil (74%); flash column chromatography (gradient elution, hexanes/EtOAc, 3:1 to 2:1); IR ($CHCl_3$) 3650–3380 (br m), 3000 (s), 2960 (s), 2930 (s), 2880 (s), 1675 (s), 1450 (s), 1270 (s), 990 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 0.99 (t, J = 7.4 Hz, 3 H), 1.72–2.05 (m, 6 H), 2.18 (q, J = 7.4 Hz, 2 H), 2.41–2.52 (m, 4 H), 2.63 (br s, 1 H), 2.77–3.07 (m, 4 H), 4.83 (s, 2 H); mass spectrum, m/e 286.1039, (M^+ calcd for $C_{14}H_{22}O_2S_2$, 286.1061).

General Procedure for Methylation of the 1,3-Dioxin Vinylogous Ester System: Preparation of 6,7-Dihydro-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one [Table V, Entry 1 (LDA, THF, MeI)]. To a stirred solution of diisopropylamine (0.65 mL, 4.60 mmol) in 8 mL of THF at 0 °C was added 1.83 mL of *n*-butyllithium (2.40 M in hexanes, 4.40 mmol). After 30 min the solution was cooled to −78 °C and vinylogous ester **4** (0.561 g, 4.00 mmol) dissolved in 4 mL of THF was added over a 5-min period. The mixture was stirred for 1 h. Methyl iodide (1.25 mL, 20.0 mmol) was then added and the reaction mixture was stirred for 1 h at −78 °C, warmed to 0 °C, and stirred for an additional 3 h, after which saturated aqueous NH_4Cl (5 mL) and ether (50 mL) were added. The aqueous layer was extracted with ether (3 × 50 mL), and the combined organic phases were washed with brine (20 mL), dried over $MgSO_4$, and concentrated in vacuo. The resultant oil was purified by flash column chromatography (hexanes/EtOAc, 2:1) to yield three products.

The first product to elute was 6,7-dihydro-6,7-dimethylcyclopenta-1,3-dioxin-5(4*H*)-one (0.034 g, 5%), a 3:1 mixture of diastereomers: TLC, R_f 0.28 (hexanes/EtOAc, 2:1); IR ($CHCl_3$) 3000 (m), 2960 (m), 2850 (m), 1690 (s), 1640 (s), 1425 (s), 1390 (m), 1305 (s), 910 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.22 (d, J = 7.5 Hz, 3 H), 1.25 (d, J = 7.1 Hz, 3 H), 2.03 (qd, J = 7.5, 2.5 Hz, 1 H), 2.47 (qdd, J = 7.1, 2.5, 2.1 Hz, 1 H), 4.46 (d, J = 2.1 Hz, 2 H), 5.21 (d, J = 5.5 Hz, 1 H), 5.29 (d, J = 5.5 Hz, 1 H); mass spectrum, m/e 169.0849 (MH^+ calcd for $C_9H_{13}O_3$, 169.0865).

The second product to elute was 6,7-dihdyro-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one (0.375 g, 61%), as a colorless oil: TLC, R_f 0.22 (hexanes/EtOAc, 2:1); IR ($CHCl_3$) 3000 (m), 1690 (m), 1640 (s), 1425 (m), 1395 (m), 1310 (m), 920 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.23 (d, J = 7.5 Hz, 3 H), 2.24 (ddt, J = 17.7, 2.4, 2.2 Hz, 1 H), 2.49 (qdd, J = 7.5, 7.1, 2.1 Hz, 1 H), 2.97 (ddt, J = 17.7, 7.1, 2.2 Hz, 1 H), 4.47 (t, J = 2.2 Hz, 2 H), 5.23 ($^1/_2$ AB q, J = 5.6 Hz, 1 H), 5.27 ($^1/_2$ AB q, J = 5.6 Hz, 1 H); mass spectrum, m/e 154.0627 (M^+ calcd for $C_8H_{10}O_3$, 154.0630).

Anal. Calcd for $C_8H_{10}O_3$: C, 62.30; H, 6.49. Found: C, 62.09; H, 6.48.

The third product to elute was 6,7-dihydro-7-methylcyclopenta-1,3-dioxin-5(4*H*)-one (0.017 g, 3%), as a light yellow oil: TLC, R_f 0.20 (hexanes/EtOAc, 2:1); IR ($CHCl_3$) 3000 (m), 1690 (m), 1640 (s), 1425 (m), 1390 (m), 1305 (m), 935 (m), 905 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.25 (d, J = 7.1 Hz, 3 H), 2.01 (dd, J = 17.9, 2.2 Hz, 1 H), 2.66 (dd, J = 17.9, 6.8 Hz, 1 H), 2.93 (qddt, J = 7.1, 6.8, 2.2, 2.0 Hz, 1 H), 4.48 (d, J = 2.0 Hz, 2 H), 5.23 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 5.26 ($^1/_2$ AB q, J = 5.5 Hz, 1 H); mass spectrum, m/e 155.0714 (MH^+ calcd for $C_8H_{11}O_3$, 155.0708).

Finally, 0.084 g (15%) was recovered of the vinylogous ester **4**.

4,6,7,8-Tetrahydro-6-methyl-5*H*-1,3-benzodioxin-5-one [Table V, Entry 11 (LDA, THF, MeI)]. Flash column chromatography (hexane/EtOAc, 3:1) afforded two compounds. The first to elute was 4,6,7,8-tetrahydro-6-methyl-5*H*-1,3-benzodioxin-5-one (78%), a white solid (mp 40–41 °C): TLC, R_f 0.34 (hexanes/EtOAc, 3:1); IR ($CHCl_3$) 3000 (m), 2920 (m), 2860 (m), 1635 (s), 1390 (s), 1230 (s), 935 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.15 (d, J = 6.9 Hz, 3 H), 1.65–1.81 (m, 1 H), 2.07 (dq, J = 13.2, 4.7 Hz, 1 H), 2.29–2.52 (m, 3 H), 4.36–4.50 (m, 2 H), 5.07 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 5.18 ($^1/_2$ AB q, J = 5.5 Hz, 1 H); mass spectrum, m/e 169.0869 (MH^+ calcd for $C_9H_{13}O_3$, 169.0865).

The second to elute was starting vinylogous ester (9.4%).

6,7,8,9-Tetrahydro-6-methycyclohepta-1,3-dioxin-5(4*H*)-one [Table V, Entry 14 (LDA, THF, MeI)]. Flash column chromatography (hexane/EtOAc, 4:1) afforded 6,7,8,9-tetrahydro-6-methylcyclohepta-1,3-dioxin-5(4*H*)-one (73%) as a colorless oil: TLC, R_f 0.49 (hexanes/EtOAc, 2:1); IR ($CHCl_3$) 3005 (m), 2940 (m), 2875 (m), 1625 (s), 1390 (m), 1280 (s), 1195 (m), 970 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.12 (d, J = 6.6 Hz, 3 H), 1.45–1.52 (m, 1 H), 1.69–2.01 (m, 3 H), 2.47–2.50 (m, 1 H), 2.59–2.68 (m, 1 H), 2.73 (dq, J = 11.8, 6.2 Hz, 1 H), 4.29 ($^1/_2$ ABXY, J = 14.6, 2.1, <0.5 Hz, 1 H), 4.56 ($^1/_2$ ABXY, J = 14.6, 1.0, 1.0 Hz, 1 H), 4.91 ($^1/_2$ AB q, J = 5.4 Hz, 1 H), 5.17 ($^1/_2$ AB q, J = 5.4 Hz, 1 H); mass spectrum, m/e 182.0930 (M^+ calcd for $C_{10}H_{14}O_3$, 182.0943).

General Procedure for Hydroxylation of the Vinylogous Ester System with 2-(Phenylsulfonyl)-3-phenyloxaziridine (28) Employing LDA [Table V, Entry 6 (LDA, DME, OA)]. To a stirred solution of diisopropylamine (1.80 mL, 12.80 mmol) in 40 mL of DME at 0 °C was added 5.0 mL of *n*-butyllithium (2.40 M in hexanes, 12.0 mmol). After 30 min the reaction was cooled to −78 °C, and a solution of 6,7-dihydro-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one (1.40 g, 9.10 mmol) dissolved in 10 mL of DME was added over a 10-min period. After 1 h a solution of 2-(phenylsulfonyl)-3-phenyloxaziridine (**28**) (4.76 g, 18.20 mmol) dissolved in 15 mL of DME was added in one portion. The reaction mixture was then stirred for 2 h at −78 °C and quenched by the addition of saturated aqueous NH_4Cl (10 mL), the aqueous layer was extracted with Et_2O (3 × 40 mL), and the combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The resultant residue upon purification by flash column chromatography (hexane/acetone 2:1) afforded two products.

The first product to elute was a 1.5:1 diastereomeric mixture [0.936 g (26%)] of an imine aldol byproduct, which could be further separated by flash column chromatography (hexane/Et_2O, 1:4). The first of these diasteromers was recrystallized from hexane/EtOAc (1:1) to afford an analytical sample (mp 144–145 °C dec): TLC, R_f 0.40 (hexane/Et_2O, 1:4); IR ($CHCl_3$) 3310 (br w), 3020 (m), 1690 (m), 1635 (s), 1395 (m), 1315 (s), 1160 (s), 900 (m), cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.48 (s, 3 H), 2.36 ($^1/_2$ AB q, J = 17.5 Hz, 1 H), 2.48 ($^1/_2$ AB q, J = 17.5 Hz, 1 H), 4.23

($^1/_2$ AB q, J = 13.8 Hz, 1 H), 4.35 ($^1/_2$ AB q, J = 13.8 Hz, 1 H), 4.85 (d, J = 8.8 Hz, 1 H), 4.85 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 5.07 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 6.81 (d, J = 8.8 Hz, 1 H), 6.85–7.45 (m, 10 H); mass spectrum, m/e 399.1120 (M^+ calcd for $C_{21}H_{21}NO_5S$, 399.1140).

Anal. Calcd for $C_{21}H_{21}NO_5S$: C, 63.14; H, 5.30; N, 3.51. Found: C, 63.27; H, 5.34; N, 3.37.

The second major diastereomer recrystallized from EtOAc (mp 174–175 °C, dec): TLC, R_f 0.32 (hexane/Et_2O, 1:4); IR ($CHCl_3$) 3260 (br w), 3202 (m), 1690 (m), 1640 (s), 1425 (m), 1310 (m), 1160 (m), 900 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.24 (s, 3 H), 2.15 ($^1/_2$ AB q, J = 18.2 Hz, 1 H), 2.76 ($^1/_2$ AB q, J = 18.2 Hz, 1 H), 4.17 ($^1/_2$ AB q, J = 14.1 Hz, 1 H), 4.34 (d, J = 5.8 Hz, 1 H), 4.35 ($^1/_2$ AB q, J = 14.1 Hz, 1 H), 5.00 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 5.16 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 6.29 (d, J = 5.8 Hz, 1 H), 7.00–7.60 (m, 10 H); mass spectrum, m/e 400.1172 (MH^+ calcd for $C_{21}H_{22}NO_5S$, 400.1218).

Anal. Calcd for $C_{21}H_{21}NO_5S$: C, 63.14; H, 5.30; N, 3.51. Found: C, 63.22; H, 5.41; N, 3.36.

The second product to elute from the original flash column chromatography was 6,7-dihydro-6-hydroxy-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one, a white solid, which could be recrystallized from hexane/EtOAc (1:1) (mp 93–94 °C): TLC, R_f 0.31 (hexanes/Et_2O, 2:1); IR ($CHCl_3$) 3550 (w), 3390 (br w), 1700 (m), 1635 (s), 1440 (m), 1315 (m), 895 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.43 (s, 3 H), 2.69 ($^1/_2$ ABX, J = 17.7, 2.1 Hz, 1 H), 2.82 ($^1/_2$ ABX, J = 17.7, 2.4 Hz, 1 H), 2.93 (br, 1 H), 4.40–4.55 (m, 2 H), 5.28 ($^1/_2$ AB q, J = 5.6 Hz, 1 H), 5.32 ($^1/_2$ AB q, J = 5.6 Hz, 1 H); mass spectrum, m/e 170.0599 (M^+ calcd for $C_8H_{10}O_4$, 170.0579).

Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.52; H, 5.87.

6,7-Dihydro-6-hydroxycyclopenta-1,3-dioxin-5(4*H*)-one [Table V, Entry 3 (LDA, DME, OA)]. Flash chromatography (CH_2Cl_2/EtOH, 20:1) afforded, in addition to the starting vinylogous ester 4 (12%), the α'-hydroxy vinylogous ester (29%) as a white solid, which was recrystallized from hexane/EtOAc (1:1) (mp 99.5–100.5 °C): TLC, R_f 0.26 (CH_2Cl_2/EtOH, 20:1); IR ($CHCl_3$) 3560 (br w), 3600–3250 (br w), 2925 (w), 1700 (m), 1620 (s), 1435 (s), 1320 (s), 900 (s) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.61 (dddd, J = 17.6, 2.6, 2.6, 2.6 Hz, 1 H), 3.02 (dddd, J = 17.6, 6.6, 2.2, 1.8 Hz, 1 H), 3.41 (br s, 1 H), 4.32 (ddd, J = 6.7, 2.6, 2.2 Hz, 1 H), 4.49 (m, 2 H), 5.24 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 5.34 ($^1/_2$ AB q, J = 5.5 Hz, 1 H); mass spectrum, m/e 156.0396 (M^+ calcd for $C_7H_8O_4$, 156.0422).

Next to elute was 0.0226 g (5%) of the γ-hydroxy vinylogous ester as a white solid, which was recrystallized from hexanes/EtOAc (1:1) (mp 109–110 °C): TLC, R_f 0.18 (CH_2Cl_2/EtOH, 20:1); IR ($CHCl_3$) 3680 (br w), 3650–3210 (br w), 3005 (w), 1700 (m), 1645 (s), 1435 (s), 1390 (m), 1300 (s), 980 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.37 ($^1/_2$ ABX, J = 17.8, 2.0 Hz, 1 H), 2.80 ($^1/_2$ ABX, J = 17.8, 6.5 Hz, 1 H), 2.91 (br s, 1 H), 4.46 ($^1/_2$ AB q, J = 15.1 Hz, 1 H), 4.53 ($^1/_2$ AB q, J = 15.1 Hz, 1 H), 4.91 (ddd, J = 6.4, 1.8, 1.5 Hz, 1 H), 5.21 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 5.38 ($^1/_2$ AB q, J = 5.5 Hz, 1 H); mass spectrum, m/e 156.0399 (M+ calcd for $C_7H_8O_4$, 156.0422).

Anal. Calcd for $C_7H_8O_4$: C, 53.85; H, 5.16. Found: C, 53.94; H, 5.17.

4,6,7,8-Tetrahydro-6-hydroxy-5*H*-1,3-benzodioxin-5-one [Table V, Entry 12 (LDA, DME, OA)]. Flash column chromatography (hexanes/EtOAc, 3:2) provided 26% of the imine aldol products as a 2.6:1 mixture of diastereomers and 58% of the 6-hydroxy vinylogous ester. The first to elute was the imine aldol product: TLC, R_f 0.69 (hexanes/EtOAc, 1:2); IR ($CHCl_3$) 3280 (w), 3010 (m), 1635 (s), 1395 (s), 1160 (s), 930 (m), 590 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.57–1.70 (m, 2 H), 1.80–1.92 (m, 1 H), 2.22–2.41 (m, 2 H), 2.58–2.67 (m, 1 H), 4.27–4.63 (diastereomers) (m, 2 H), 5.09 (s, 2 H), 6.27 (d, J = 4.8 Hz, 1 H), 6.94–7.60 (m, 10 H); mass spectrum, m/e 400.1279 (MH^+ calcd for $C_{21}H_{22}NO_5S$, 400.1218).

The second to elute was 58% of a colorless solid, which could be recrystallized from hexanes/EtOAc (1:1) (mp 138–140 °C): TLC, R_f 0.40 (hexanes/EtOAc, 1:2); IR ($CHCl_3$) 3580–3380 (br s), 3005 (w), 2880 (w), 1660 (m), 1635 (s), 1420 (m), 1235 (s), 930 (s) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.88 (dddd, J = 12.6, 11.2, 6.6, 5.0, 1 H), 2.35–2.63 (m, 3 H), 3.72 (d, J = 1.2 Hz, 1 H), 4.09 (ddd, J = 13.1, 5.4, 1.2 Hz, 1 H), 4.38 ($^1/_2$ ABXY, J = 14.5, 2.0, <0.5 Hz, 1 H), 4.57 ($^1/_2$ ABXY, J = 14.5, 2.0, 1.9 Hz, 1 H), 5.07 ($^1/_2$ AB q, J = 5.6 Hz, 1 H), 5.26 ($^1/_2$ AB q, J = 5.6 Hz, 1 H); mass spectrum, m/e 170.0594 (M^+ calcd for $C_8H_{10}O_4$, 170.0579).

6,7,8,9-Tetrahydro-6-hydroxycyclohepta-1,3-dioxin-5-(4*H*)-one [Table V, Entry 15 (LDA, DME, OA)]. Flash column chromatography of the reaction residue (hexane/EtOAc, 2:1) afforded 20% of vinylogous ester 6.

The next to elute was the imino aldol products (18%) as a colorless oil: TLC, R_f 0.30 (hexanes/EtOAc, 2:1); IR ($CHCl_3$) 3550 (br w), 3490–3200 (br m), 3010 (m), 2870 (m), 1615 (s), 1450 (m), 1395 (s), 1160 (s), 970 (s), 590 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.63–2.10 (m, 4 H), 2.45–2.62 (m, 2 H), 3.06 (ddd, J = 11.1, 7.1, 4.1 Hz, 1 H), 4.04 ($^1/_2$ ABX, J = 14.4, 1.6 Hz, 1 H), 4.45 ($^1/_2$ ABX, J = 14.4, 1.4 Hz, 1 H), 4.58 (dd, J = 9.2, 4.0 Hz, 1 H), 4.79 ($^1/_2$ AB q, J = 5.5 Hz, 1 H); 5.12 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 6.69 (d, J = 9.2 Hz, 1 H), 6.99–7.59 (m, 10 H); mass spectrum, m/e 413.1303 (M^+ calcd for $C_{22}H_{23}NO_5S$, 413.1297).

The next compound to elute was 6,7,8,9-tetrahydro-6-hydroxycyclohepta-1,3-dioxin-5(4*H*)-one (54%), a white solid, which was recrystallized from hexane/EtOAc (4:1) to yield an analytical sample (colorless plates, mp 67–69 °C): TLC, R_f 0.27 (hexanes/EtOAc, 2:1); IR ($CHCl_3$) 3600–3300 (br w), 3000 (w), 2880 (w), 1620 (s), 1375 (s), 1300 (m), 960 (m), 890 (m) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.55–1.72 (m, 2 H), 2.00–2.12 (m, 1 H), 2.25–2.39 (m, 1 H), 2.57 (ddd, J = 17.1, 4.5, 4.0 Hz, 1 H), 2.60–2.72 (m, 1 H), 4.15 (d, J = 3.8 Hz, 1 H), 4.20 (ddd, J = 11.3, 6.4, 3.8 Hz, 1 H), 4.41 ($^1/_2$ ABXY, J = 4.6, 0.9, 0.8 Hz, 1 H), 4.58 ($^1/_2$ ABXY, J = 4.6, 0.9, 0.8 Hz, 1 H), 5.02 ($^1/_2$ AB q, J = 5.6 Hz, 1 H), 5.20 ($^1/_2$ AB q, J = 5.6 Hz, 1 H); mass spectrum, m/e 184.0743 (M^+ calcd for $C_9H_{12}O_4$, 184.0735).

General Procedure for the Hydroxylation of the Vinylogous Ester System with 2-(Phenylsulfonyl)-3-phenyloxaziridine (28). Employing NaHMDS [Table V, Entry 4 (NaHMDS, THF, OA)]. To a solution composed of 0.600 mL of sodium bis(trimethylsilyl)amide (1.0 M in hexanes, 0.600 mmol) and 5 mL of THF, cooled to −78 °C, was added vinylogous ester 4 (0.070 g, 0.500 mmol) dissolved in 1 mL of THF. The reaction mixture was allowed to stir for 1 h, after which time 2-(phenylsulfonyl)-3-phenyloxaziridine (28) (0.261 g, 1.00 mmol) dissolved in 2 mL of THF was added over a period of 10 min. After an additional 1.5 h the reaction was quenched at −78 °C by the addition of saturated aqueous NH_4Cl (5 mL). The aqueous phase was extracted with ether (3 × 25 mL), and the combined organic phases were dried and concentrated in vacuo to give a pale yellow oil. Flash column chromatography (CH_2Cl_2/EtOH, 20:1) afforded, in addition to the starting vinylogous ester 4 (19%), 0.0218 g (28%) of 6,7-dihdyro-6-hydroxycyclopenta-1,3-dioxin-5(4*H*)-one (vide supra): TLC, R_f 0.26 (CH_2Cl_2/EtOH, 20:1).

The next compound to elute was 6,7-dihydro-7-hydroxycyclopenta-1,3-dioxin-5(4*H*)-one (0.0226 g, 28%) (vide supra): TLC, R_f 0.18 (CH_2Cl_2/EtOH, 20:1).

6,7-Dihydro-6-methyl-7-hydroxycyclopenta-1,3-dioxin-5-(4*H*)-one [Table V, Entry 7 (NaHMDS, THF, OA)]. Flash column chromatography afforded 4% of 6-hydroxy-6-methyl vinylogous ester (vide supra): TLC, R_f 0.34 (CH_2Cl_2/EtOH, 20:1).

Next to elute was 76% of 6,7-dihydro-6-methyl-7-hydroxycyclopenta-1,3-dioxin-5(4*H*)-one, a 3:1 mixture of diastereomers which was not separated: TLC, R_f 0.27 (CH_2Cl_2/EtOH, 20:1); IR ($CHCl_3$) 3590 (w), 3590–3200 (br w), 3000 (m), 1700 (m), 1655 (s), 1430 (s), 1390 (m), 1310 (s), 910 (s) cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.20, 1.29 (diastereomers) (d, J = 7.7 Hz, 3 H), 2.41 (d, J = 4.3 Hz, 1 H), 2.66 (dq, J = 6.8, 0.8 Hz, 1 H), 4.42–4.55 (m, 3 H), 5.18–5.24 (m, 1 H), 5.36–5.41 (m, 1 H); mass spectrum, m/e 170.0567 (M^+ calcd for $C_8H_{10}O_4$, 170.0579).

4,6,7,8-Tetrahydro-8-hydroxy-5*H*-1,3-benzodioxin-5-one [Table V, Entry 13 (NaHMDS, THF, OA)]. Flash column chromatography (hexane/EtOAc, 3:2) yielded 49% of 4,6,7,8-tetrahydro-8-hydroxy-5*H*-1,3-benzodioxin-5-one (vide supra): TLC, R_f 0.40 (hexane/EtOAc, 1:2).

The second compound to elute was 4,6,7,8-tetrahydro-8-hydroxy-5*H*-1,3-benzodioxin-5-one (37%) as a colorless solid, which was recrystallized from hexanes/EtOAc (1:1) to give an analytical sample (mp 54–56 °C): TLC, R_f 0.21 (hexanes/EtOAc, 1:2); IR ($CHCl_3$) 3600–3250 (br w), 3590 (w), 3005 (m), 1645 (s), 1400 (m), 1260 (s), 1070 (m), 955 (s) cm^{-1}; ^{1}H NMR (250 MHz,

$CDCl_3$) δ 1.25 (br s, 1 H), 2.01–2.10 (m, 1 H), 2.72–2.42 (m, 2 H), 2.55–2.63 (m, 2 H), 4.45 (dd, J = 2.0, 1.7 Hz, 1 H), 4.52 (d, J = 3.9 Hz, 1 H), 5.19 ($^1/_2$ AB q, J = 5.5 Hz, 1 H), 5.22 ($^1/_2$ AB q, J = 5.5 Hz, 1 H); mass spectrum, m/e 170.0575 (M^+, calcd for $C_8H_{10}O_4$, 170.0579).

6,7,8,9-Tetrahydro-9-hydroxycyclohepta-1,3-dioxin-5-(4*H*)-one [Table V, Entry 16 (NaHMDS, THF, OA)]. Flash column chromatography (hexanes/EtOAc, 1:1) afforded two products. The first to elute was 6,7,8,9-tetrahydro-9-hydroxycyclohepta-1,3-dioxin-5(4*H*)-one (51%) (vide supra): TLC, R_f 0.27 (hexanes/EtOAc, 2:1).

The second to elute was 6,7,8,9-tetrahydro-9-hydroxycyclohepta-1,3-dioxin-5(4*H*)-one (37%), a colorless oil: TLC, R_f 0.10 (hexanes/EtOAc, 2:1); IR ($CHCl_3$) 3600–3280 (br w), 3580 (w), 3000 (w), 2880 (w), 1620 (s), 1380 (m), 1225 (s), 980 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.80–2.21 (m, 4 H), 2.53 (ddd, J = 16.0, 8.1, 5.1 Hz, 1 H), 2.71 (br s, 1 H), 2.78 (ddd, J = 16.0, 7.4, 4.8 Hz, 1 H), 4.45 (d, J = 1.4 Hz, 2 H), 4.58 (br s, 1 H), 5.13 ($^1/_2$ AB q, J = 5.3 Hz, 1 H), 5.17 ($^1/_2$ (AB q, J = 5.3 Hz, 1 H); mass spectrum, m/e 184.0750 (M^+ calcd for $C_9H_{12}O_4$, 184.0735).

General Procedure for Hydroxylation of the Vinylogous Ester System with (Camphorylsulfonyl)oxaziridine (29) [Table V, Entry 9 (LDA, THF, COA)]. To a stirred solution of diisopropylamine (8.5 mL, 60.0 mmol) in 450 mL of THF at −45 °C was added 23.5 mL of *n*-butyllithium (2.24 M, 52.6 mmol). After 1 h the reaction was cooled to −85 °C and a solution of 6,7-dihydro-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one (7.71 g, 50.0 mmol) dissolved in 25 mL of THF was added over a 15-min period. After 1 h at −80 °C a solution of the (camphorylsulfonyl)oxaziridine **29** (13.7 g, 60.0 mmol) dissolved in 125 mL of THF was added over a 15-min period. The mixture was stirred at −80 °C for 1 h, brought to −45 °C (0.5 h), and stirred at −45 °C for 1 h. The reaction was quenched by the addition of 10 mL of saturated aqueous NH_4Cl and then brought to room temperature. The solvents were removed in vacuo, and to the residue were added chloroform (500 mL) and water (15 mL). The mixture was shaken vigorously, the layers were separated, and the aqueous layer was extracted with chloroform (3 × 75 mL). The combined organic phases were dried over Na_2SO_4 and concentrated in vacuo. Purification of the resultant residue by flash column chromatography ($CHCl_3$/acetone, 4:1, and then CH_2Cl_2/EtOH, 20:1) afforded two products.

The first product to elute was 6,7-dihydro-6-hydroxy-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one (vide supra) (68%): TLC, R_f 0.34 (CH_2Cl_2/EtOH, 20:1); $[\alpha]^{26}_D$ +7.3° (c 0.60, $CHCl_3$). A ^1H NMR chiral shift reagent study using Eu(hfc)$_3$ showed an enantiomeric excess of 16%.

The next to elute was 6,7-dihydro-7-hydroxy-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one (vide supra) (4%), a 3:1 mixture of diastereomers, which was not separated: TLC, R_f 0.27 (CH_2Cl_2/EtOH, 20:1).

6,7-Dihydro-7-hydroxy-6-methylcyclopenta-1,3-dioxin-5-(4*H*)-one [Table V, Entry 10 (NaHMDS, THF, COA)]. Flash column chromatography ($CHCl_3$/acetone, 4:1, and then CH_2Cl_2/EtOH, 20:1) of the reaction residue provided two products.

The first to elute was 6,7-dihydro-6-hydroxy-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one (vide supra) (3%): TLC, R_f 0.34 (CH_2Cl_2/EtOH, 20:1).

The next to elute was 6,7-dihydro-7-hydroxy-6-methylcyclopenta-1,3-dioxin-5(4*H*)-one (vide supra) (28%), a 3:1 mixture of diastereomers, which was not separated: TLC, R_f 0.27 (CH_2Cl_2/EtOH, 20:1).

6,7-Dihydro-6-hydroxycyclopenta-1,3-dioxin-5(4*H*)-one [Table V, Entry 8 (LDA, THF, COA)]. Flash column chromatography ($CHCl_3$/acetone, 4:1, and then CH_2Cl_2/EtOH, 20:1) provided starting vinylogous ester (19%) and two other products.

The first to elute was 6,7-dihydro-6-hydroxycyclopenta-1,3-dioxin-5(4*H*)-one (vide supra) (37%): TLC, R_f 0.26 (CH_2Cl_2/EtOH, 20:1); $[\alpha]^{26}_D$ +3.9° (c 0.69, $CHCl_3$). Esterification with (*S*)-(+)-*O*-methylmandelic acid provided a diastereomeric mixture and integration of resonances in the ^1H NMR spectrum of this mixture showed that the alcohol was produced with an enantiomeric excess of 14%.

The next to elute was 6,7-dihydro-7-hydroxycyclopenta-1,3-dioxin-5(4*H*)-one (vide supra) (3%): TLC, R_f 0.18 (CH_2Cl_2/EtOH, 20:1).

General Procedure for 1,3-Carbonyl Transposition of the Hydroxy Vinylogous Ester System Using $LiAlH_4$: Preparation of 4-Hydroxy-2-(hydroxymethyl)-2-cyclohexenone. To a stirred solution of 4,6,7,8-tetrahydro-6-hydroxy-5*H*-1,3-benzodioxin-5-one (0.0408 g, 0.240 mmol) in 2 mL of THF cooled to 0 °C was added dropwise 0.36 mL of a solution of $LiAlH_4$ (1.0 M in ether, 0.360 mmol). The reaction mixture was allowed to warm to room temperature, stirred for 2 h, cooled back to 0 °C, and then quenched by the addition of saturated aqueous Na_2SO_4 (0.5 mL). The insoluble salts were removed by filtration, and the filtrate was concentrated in vacuo. The resultant oil was then dissolved in 2 mL of THF and 0.2 mL of 2 N HCl added. After 15 min, the reaction was neutralized with aqueous K_2CO_3, diluted with ether, dried over $MgSO_4$, filtered, and evaporated. Flash column chromatography (EtOAc) provided 0.0231 g (68%) of the diol, as a colorless oil: TLC, R_f 0.20 (EtOAc); IR ($CHCl_3$) 3590 (w), 3550–3280 (br m), 1675 (s), 1370 (m), 1050 (m), 1005 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.94–2.04 (m, 1 H), 2.30–2.47 (m, 2 H), 2.65 (ddd, J = 9.1, 7.7, 4.9 Hz, 1 H), 2.96 (br d, J = 8.5 Hz, 2 H), 4.25 (br s, 2 H), 4.59 (br s, 1 H), 6.89 (dd, J = 1.3, 1.2 Hz, 1 H); mass spectrum, m/e 143.0717 (MH^+ calcd for $C_7H_{11}O_3$, 143.0708).

6-Hydroxy-2-(hydroxymethyl)-2-cyclohexenone. Flash column chromatography (EtOAc) provided the diol (62%) as a colorless oil: TLC, R_f 0.32 (EtOAc); IR ($CHCl_3$) 3650–3180 (br m), 3590 (w), 3000 (w), 2920 (w), 1670 (s), 1350 (m), 1235 (m), 1050 (m), 1005 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.85–1.99 (m, 2 H), 2.36–2.44 (m, 1 H), 2.51–2.59 (m, 2 H), 3.76 (br s, 1 H), 4.22 (dd, J = 13.8, 5.6 Hz, 1 H), 4.31 (d, J = 0.9 Hz, 2 H), 6.98 (ddd, J = 2.9, 1.7, 1.2 Hz, 1 H); mass spectrum, m/e 142.0629 (M^+ calcd for $C_7H_{10}O_3$, 142.0630).

4-Hydroxy-2-(hydroxymethyl)-2-cycloheptenone. Flash column chromatography (EtOAc) provided the diol (62%) as a colorless oil: TLC, R_f 0.23 (EtOAc); IR ($CHCl_3$) 3650–3100 (br s), 3000 (m), 2940 (s), 1660 (s), 1380 (m), 1225 (m), 1030 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.70–1.91 (m, 3 H), 2.16 (ddd, J = 10.7, 5.6, 5.1 Hz, 1 H), 2.47–2.67 (m, 2 H), 3.48 (br s, 2 H), 4.24 (br s, 2 H), 4.61 (br s, 1 H), 6.70 (d, J = 2.0 Hz, 1 H); mass spectrum, m/e 157.0852 (MH^+ calcd for $C_8H_{13}O_3$, 157.0865).

7-Hydroxy-2-(hydroxymethyl)-2-cycloheptenone. Flash column chromatography (hexanes/EtOAc, 1:3) provided the diol (71%) as a colorless oil: TLC, R_f 0.38 (EtOAc); IR ($CHCl_3$) 3650–3250 (br m), 3000 (m), 2925 (s), 2875 (m), 1710 (w), 1660 (s), 1375 (m), 1240 (m), 1030 (s) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 1.57–1.70 (m, 2 H), 1.98–2.03 (m, 1 H), 2.23–2.54 (m, 3 H), 3.96 (br s, 2 H), 4.30 ($^1/_2$ AB q, J = 6.8 Hz, 1 H), 4.34 ($^1/_2$ AB q, J = 6.8 Hz, 1 H), 4.41 (m, 1 H), 6.93 (ddd, J = 6.1, 5.0, 2.0 Hz, 1 H); mass spectrum, m/e 156.0801 (M^+ calcd for $C_8H_{12}O_3$, 156.0786).

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(n = 0, R^1 = Me, R^2 = OH), 114908-71-3; (+)-**B** (n = 0, R^1 = Me, R^2 = OH), 114908-88-2; (±)-**B** (n = 1, R^1 = H, R^2 = Me), 114908-67-7; (±)-**B** (n = 2, R^1 = H, R^2 = Me), 114908-68-8; (±)-(R^*,R^*)-**B** (n = 0, R^1 = Me, R^2 = CH(Ph)$NHSO_2Ph$), 114908-69-9; (±)-(R^*,S^*)-**B** (n = 0, R^1 = Me, R^2 = CH(Ph)$NHSO_2Ph$), 114908-70-2; (±)-(R^*,R^*)-**B** (n = 1, R^1 = H, R^2 = CH(Ph)$NHSO_2Ph$), 114908-74-6; (±)-(R^*,S^*)-**B** (n = 1, R^1 = H, R^2 = CH(Ph)$NHSO_2Ph$), 114908-75-7; (±)-(R^*,R^*)-**B** (n = 2, R^1 = H, R^2 = CH(Ph)$NHSO_2Ph$), 114908-77-9; (±)-(R^*,S^*)-**B** (n = 2, R^1 = H, R^2 = CH(Ph)$NHSO_2Ph$), 114908-78-0; (±)-*cis*-**C** (n = 0, R^1 = R^2 = Me), 114908-63-3; (±)-*trans*-**C** (n = 0, R^1 = R^2 = Me), 114908-64-4; (±)-**C** (n = 0, R^1 = H, R^2 = Me), 114908-66-6; (±)-*cis*-**C** (n = 0, R^1 = Me, R^2 = OH), 114908-80-4; (±)-*trans*-**C** (n = 0, R^1 = Me, R^2 = OH), 114908-81-5; 2-(hydroxymethyl)-2-cyclopentenone, 68882-71-3; 2-(hydroxymethyl)-2-cyclohexenone, 105956-40-9; 2-(hydroxymethyl)-2-cycloheptenone, 114908-52-0; 2-(hydroxymethyl)-3-*n*-butyl-2-cyclopentenone, 114908-53-1; 2-(hydroxymethyl)-3-*n*-butyl-2-cyclohexenone, 114908-54-2; 2-(hydroxymethyl)-3-*n*-butyl-2-cycloheptenone, 114908-55-3; 2-(hydroxymethyl)-3-phenyl-2-cyclopentenone, 114908-56-4; 2-(hydroxymethyl)-3-phenyl-2-cyclohexenone, 114908-57-5; 2-(hydroxymethyl)-3-phenyl-2-cycloheptenone, 114908-58-6; 2-(hydroxymethyl)-3-vinyl-2-cyclopentenone, 114908-59-7; 2-(hydroxymethyl)-3-vinyl-2-cyclohexenone, 114908-60-0; 2-(hydroxymethyl)-3-vinyl-2-cycloheptenone, 114908-61-1; 2-lithio-2-ethyl-1,3-dithiane, 53178-38-4; 2-(hydroxymethyl)-3-(2-ethyl-1,3-dithian-2-yl)-2-cyclohexenone, 114929-05-4; 2-(hydroxymethyl)-3-(2-ethyl-1,3-dithian-2-yl)-2-cyclopentenone, 114929-06-5; 2-(hydroxymethyl)-3-(2-ethyl-1,3-dithian-2-yl)-2-cycloheptenone, 114908-62-2.

Diels–Alder Reactions of Cycloalkenones. 14. Endo Diastereoselectivity of 2-Cyclohexenones in Reactions with Cyclopentadiene[1]

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Aluminum chloride catalyzed Diels–Alder reactions of 2-cyclohexenones with cyclopentadiene are described. Structure analysis of the adducts by standard means and ^{13}C NMR spectroscopy is presented. The endo–exo diastereoselectivity of the above and earlier reactions is discussed.

A priori the two components of a Diels–Alder reaction may interact in two different orientations, affording endo and exo adducts. Often, however, only the endo adduct is formed. This fact was explained first by the Alder–Stein rule[3] of maximum accumulation of double bonds and later by stabilizing second-order orbital interactions,[4] inductive[5] or charge-transfer[6] interactions, and also geometrical overlap relationship of the π-orbitals at the primary centers.[7] Deviation from the endo rule was ascribed usually to steric factors.[8]

In a previous study[9] this aspect of the Diels–Alder reaction was investigated with catalyzed cycloadditions of 2-cyclohexenones with (*E*)-piperylene. The results showed that the presence of a methyl group at the olefinic α-carbon of the dienophile increases markedly the exo selectivity of the reaction. Whereas the reaction of 2-cyclohexenone is fully endo-selective, that of 2-methyl-2-cyclohexenone gives a 2.3:1 mixture of the endo and exo adducts. Similarly, the cycloadditions of 2-cyclohexenones substituted only at carbons 4 or 5 are fully endo-diastereoselective, but the reactions of the corresponding 2-methyl-2-cyclohexenones give mixtures of endo and exo adducts. A similar methyl effect was observed earlier in the thermal cycloadditions of dienophilic ethylenes with cyclopentadiene.[10–12]

In continuation of the above study, an investigation of aluminum chloride catalyzed reactions of cyclopentadiene

Table I. Aluminum Chloride Catalyzed Diels–Alder Reactions of Cyclohexenones 2–4 with Cyclopentadiene[a] and (*E*)-Piperylene[b]

	cyclopentadiene[d]			(*E*)-piperylene[d]	
dienophile	products	endo	exo	endo	exo
2a	**5a, 6a**	89	11	>97	
3a	**7a, 8a**	30	70	70[c]	30
2b	**5b, 6b**	95	5	>97	
3b	**7b, 8b**	60	40	>97	
2c	**5c, 6c**	79	21	>99	
3c	**7c, 8c**	29	71	>97	
4	**9, 10**	42	58	78	22

[a] Reaction conditions reported in Table III. [b] Reference 9. [c] Valenta and co-workers[13] reported a 78:22 mixture of endo and exo adducts for the reaction catalyzed by aluminum chloride. [d] Percent, GLC-based.

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