Photoadditions and Dialkylcuprate Additions to 2-*tert*-Butyl-2,6-dimethyl-1,3-dioxin-4-one and Related Heterocycles. Experimental, *Ab Initio* Theoretical, and X-ray Structural Studies of Facial Selectivity and Enone Pyramidalization[1]

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Abstract: Preparation and ground-state reactions of 1,3-dioxinone (**1**), α,β-unsaturated δ-lactone **4**, and dihydropyranone **5** are reported. These three substrates have identical alkyl substituents but differ in the number and placement of oxygen atoms in the heterocycle. Reaction of **1** or **4** with $(n\text{-Bu})_2\text{CuLi}$ leads to exclusive addition on the *top* face (side opposite the *tert*-butyl group) of the substrate while addition to **5** gives a 50:50 mixture of diastereomers. Pyramidalizations of the enone portions of **1**, **4**, and **5** (along with 2-cyclohexenone) have been predicted using *ab initio* Hartree–Fock (HF) methods with a split-valence plus polarization basis set, 6-31G*, and with the inclusion of electron correlation by Møller–Plesset perturbation theory (MP2). These predictions have been compared with the results of X-ray crystal structure determinations on related heterocycles which were present in the Cambridge Crystallographic Database. Both theoretical methods indicate that the extent of pyramidalization decreases in the following order: 1,3-dioxinones > α,β-unsaturated δ-lactones > dihydropyranones > 2-cyclohexenones. This trend suggests that the facial selectivity observed in the ground-state reactions of **1**, **4**, and **5** is related to the extent of pyramidalization in the enone portion of these substrates. Photoaddition reactions of **1** with various cycloalkenes are also reported. The exclusive or major product in these reactions results from attack on the *bottom* face of **1**. Thus, substrate **1** allows exclusive entry of ground-state reactants on the *top* face, but excited-state reactions occur exclusively or primarily on the *bottom* face.

Introduction

This report describes the chemistry of 2-*tert*-butyl-2,6-dimethyl-1,3-dioxin-4-one (**1**), a substrate which allows certain ground-state reactions to take place on one face with complete selectivity but allows excited-state reactions to take place on the *opposite* face with complete or high selectivity. In an attempt to understand the selectivities of this dioxinone, we have also examined reactions of, X-ray crystallographic structures of, and theoretical predictions on related oxygen-containing heterocycles.

Seebach described the preparation[2] and reactions[3] of 2-*tert*-butyl-6-methyl-1,3-dioxin-4-one (**2**). The compound **2** underwent conjugate addition reactions with reagents such as dialkylcuprates and thiophenoxide to give a single diastereomer in which the nucleophile was introduced on the same face of the ring as the acetal hydrogen on C-2. Similarly, catalytic hydrogenation took place on the face *anti* to the *tert*-butyl group at the acetal center.[3] Sato reported[4] that cuprate addition to the spirodioxinone **3a** (prepared from menthone) occurred preferentially on the face opposite the isopropyl group [diastereomeric excess (de) 82%] and catalytic hydrogenation of **3b** also took place primarily on this face (de 88%).

Conversely, photoaddition of alkenes to various chiral dioxinones has been reported to occur preferentially on the *more* hindered face. For example, photoaddition of cyclopentene to either **3a**[4] or **3b**[5] gave primarily, but not exclusively, the *cis-anti-cis* adducts formed by reaction on the *same* face as the isopropyl substituent. Also, photoaddition of cyclopentene to 2-cyclohexyl-1,3-dioxin-4-one at −78 °C gave a slight preference for reaction on the same face as the cyclohexyl group.[6] Dioxinone **2** upon irradiation with cyclohexene was reported to give a mixture of at least four diastereomers,[7] but their structures were not determined.

Very little work has been reported on the preparation and reactions of dioxinones such as **1**, which possess a dialkyl chiral center at C-2. Herein we describe the impressive diastereoselectivities which are possible with **1** (as compared to **2**) in both ground- and excited-state reactions. The preparation and reactions of related heterocycles, namely the α,β-unsaturated δ-lactone **4** and the dihydropyranone **5**, are also described in an effort to rationalize the selectivity achieved with **1**. Finally, high-level theoretical predictions of the geometries of all three classes of heterocycles and of 2-cyclohexenone are reported with emphasis on the pyramidalization of the enone system in each substrate. In addition, structures taken from the Cambridge Crystallographic Database for the four classes of compounds are compared with the theoretical results.

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‡ University of Waterloo.
⊕ Abstract published in *Advance ACS Abstracts*, March 15, 1994.
(1) A preliminary account of a portion of this work has been published: Lange, G.L.; Organ, M. G. *Tetrahedron Lett.* **1993**, *34*, 1425.
(2) (a) Zimmermann, J.; Seebach, D. *Helv. Chim. Acta* **1987**, *70*, 1104. (b) Seebach, D.; Gysel, U.; Job, K.; Beck, A. K. *Synthesis* **1992**, 39.
(3) Seebach, D.; Zimmermann, J.; Gysel, U.; Ziegler, R.; Ha, T.-K. *J. Am. Chem. Soc.* **1988**, *110*, 4763.
(4) Sato, M.; Takayama, K.; Furuya, T.; Inukai, N.; Kaneko, C. *Chem. Pharm. Bull.* **1987**, *35*, 3971.
(5) Demuth, M.; Palomer, A.; Sluma, H.-D.; Dey, A. K.; Kruger, C.; Tsay, Y.-H. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1117.
(6) Sato, M.; Abe, Y.; Kaneko, C. *J. Chem. Soc., Perkin Trans 1* **1990**, 1779.
(7) Seebach, D.; Zimmermann, J. *Helv. Chim. Acta* **1986**, *69*, 1147.

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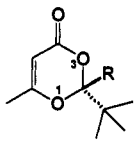
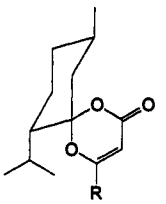
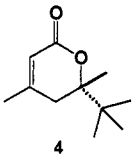


1, R = Me; 2, R = H



3a, R = H; 3b, R = Me



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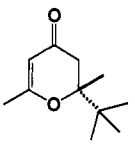

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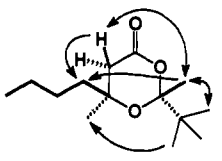
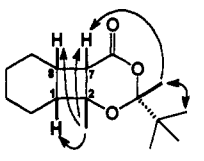
Results and Discussion

Reactions of 1. Dioxinone **1** was prepared in racemic form by reaction of pinacolone and diketene[8] and in optically pure form (R = CD_3) from the readily available (*R*)-3-hydroxybutyric acid[9] using a recently described procedure.[10] Reaction of **1** with $(n\text{-Bu})_2CuLi$ gave **6a** in 73% yield while reaction with $Et_2CuMgBr$ gave **6b** (Scheme 1) in 57% yield (83% based on recovered **1**). None of the other diastereomers was observed in the ^1H NMR spectra of the crude or purified products in either reaction. The stereochemistries of **6a** and **6b** were determined by NOE difference experiments (Figure 1). Thus, in both reactions the only isomer formed resulted from attack of the cuprate reagent on the top face of **1**. Hydrogenation of **1** was investigated using catalysts such as Pd/C, PtO_2, and Rh/alumina at various hydrogen pressures, but the dioxinone either did not react or fragmented.

The photoaddition reactions of **1** were investigated using three cycloalkenes. Irradiation through a Corex filter of **1** and cyclohexene in 20% acetone/acetonitrile[11] gave a mixture of three crystalline adducts: **7a** (54%), **8** (15%), and **9a** (15%) (Scheme 2). The structure of **7a** was determined by single-crystal X-ray analysis.[12] The structures of **8** and **9a** were established by detailed analyses of their ^1H and ^{13}C NMR spectra and by NOE difference experiments (see Figure 1). In the ^1H NMR spectra of **7a** and **8**, the H-7/H-8 coupling constant was 4.4 Hz for the *anti* adduct and 10.2 Hz for the *syn* adduct. Normally the *cis* vicinal coupling constant for cyclobutane protons is larger than the *trans*,[13] but caution must be exercised when making such assignments for more flexible or highly substituted adducts.[14] In the ^{13}C NMR spectra (see Experimental Section), the downfield shift of the cyclobutane carbons in **9a** as compared to **7a** and **8** was indicative of a *trans* ring fusion in the former adduct.[15-17]



6a



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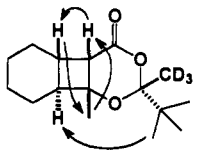
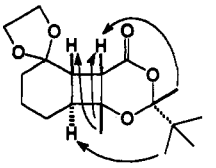
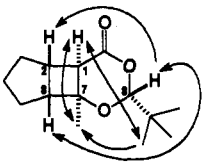


9a



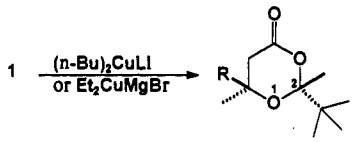
9b



14b

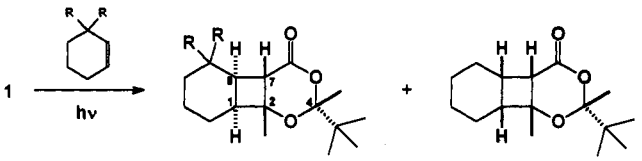
Figure 1. Selected NOE difference experiments. The arrows point from the proton(s) being irradiated to the proton(s) which exhibited the enhancement. Double-headed arrows indicate the experiment was done in both directions. It was necessary to use the 4-CD_3 isomer of **9a**, as the 2- and 4-methyl resonances were coincident.

Scheme 1



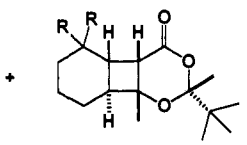
6a, R = n-Bu
6b, R = Et

Scheme 2



7a, R=H
7b, RR = OCH_2CH_2O

8



9a, R = H
9b, RR = OCH_2CH_2O

Photoaddition of **1** and the ethylene ketal of 2-cyclohexenone gave a mixture of head-to-head adducts **7b** (35%) and **9b** (14%) (Scheme 2). The H-7/H-8 coupling constant of 4.0 Hz in the ^1H NMR spectrum of **7b** is consistent with the assigned *anti* stereochemistry, and NOE enhancements of the H-1 and H-8 signals upon irradiation of the *tert*-butyl group supported the proposed relative stereochemistry. NOE difference experiments with **9b** (Figure 1) showed that irradiation of the *tert*-butyl group resulted in enhancement of H-1 and 4-methyl resonances while irradiation of the 2-methyl group showed enhancement of H-7, H-8, and the 4-methyl signals. These experiments confirmed the *cis*, *trans* stereochemistry assigned to the ring fusions in **9b**. In

(8) Prepared in 76% yield by heating diketene (1 equiv) with pinacolone (2 equiv) in the presence of *p*-TsOH, as described previously for the synthesis of 2,2,6-trimethyl-1,3-dioxin-4-one: Carroll, M. F.; Bader, A. R. *J. Am. Chem. Soc.* **1952**, *74*, 6305.

(9) Seebach, D.; Beck, A. K.; Breitschuh, R.; Job, K. *Org. Synth.* **1992**, *71*, 39.

(10) Lange, G. L.; Organ, M. G.; Roche, M. R. *J. Org. Chem.* **1992**, *57*, 6000. The use of the CD_3 group is a necessary part of the preparation of optically active **1**, as advantage is taken of a deuterium isotope effect in a regioselective bromination step.

(11) Baldwin, S. W.; Wilkinson, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 3634.

(12) See Experimental Section and supplementary material for details.

(13) (a) Rinaldi, P. L.; Salomon, R. G. *J. Org. Chem.* **1983**, *48*, 3182. (b) Bourhis, M.; Goursolle, M.; Leger, J.-M.; Duboudin, J.-G.; Duboudin, F.; Picard, P. *Tetrahedron Lett.* **1989**, *30*, 4665. (c) Lewis, F. D.; Barancyk, S. V. *J. Am. Chem. Soc.* **1989**, *111*, 8653.

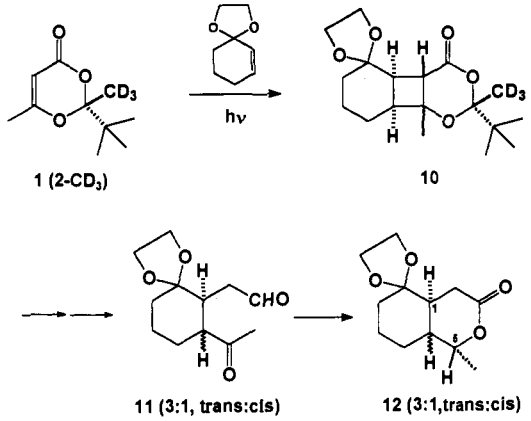
(14) Lange, G. L.; Organ, M. G.; Lee, M. *Tetrahedron Lett.* **1990**, *31*, 4689.

(15) Williams, J. R.; Lin, C.; Chodosh, D. F. *J. Org. Chem.* **1985**, *50*, 5815.

(16) Whitesell, J. K.; Minton, M. A. *Stereochemical Analysis of Alicyclic Compounds by C-13 NMR Spectroscopy*; Chapman and Hall: New York, 1987; p 190.

(17) Metzger, P.; Cabestaing, C.; Casadevall, E.; Casadevall, A. *Org. Magn. Reson.* **1982**, *19*, 144.

Scheme 3



the ^{13}C NMR spectra of these adducts, the C-10 to C-12 resonances in **9b** appeared considerably further downfield (37.4, 25.5, 24.4 ppm, respectively) than those in **7b** (32.1, 20.0, 19.8 ppm). Such downfield shifts of methylene carbon atoms in related *trans*-fused systems have been reported.[17] Adducts in which a *trans* ring fusion is found in the alkene portion of the product (as opposed to the enone portion) are not common, but previous examples (including one derived from an unsaturated ketal) have been reported.[18] In the ^1H NMR spectra of **7b** and **9b**, two singlets for the 2- and 4-methyl groups were present in the region 1.4–1.5 ppm. To distinguish between these two methyl groups, a sample of **1**, in which the 2-methyl group was deuterated, was irradiated along with the cyclohexenone ketal. The methyl resonance not present in the ^1H NMR spectrum of each of the deuterated adducts or broadened in the ^{13}C NMR spectrum was assigned to the 4-methyl group (see Experimental Section).

To illustrate the potential for asymmetric induction in these systems, optically pure dioxinone **1** (R = CD_3)[10] was irradiated along with the ketal of 2-cyclohexenone and the major adduct **10** was isolated (Scheme 3). Reduction of **10** at −78 °C with diisobutylaluminum hydride gave a lactol which upon mild hydrolysis gave deuterated pinacolone and keto aldehyde **11** as a 3:1 mixture of epimers.[11] Treatment of **11** with diisobutylaluminum methoxide using our previously reported intramolecular Tishchenko methodology[19] gave an inseparable 3:1 mixture of δ-lactones **12**. The ^1H NMR spectrum of the *trans* lactone (the major component in the mixture) was examined in the presence of the chiral solvating agent (CSA) (*S*)-(+)-2-(trifluoromethyl)-1-(9-anthryl)ethanol[20] with particular attention being directed to the doublet for the 5-methyl group. The spectrum of a racemic sample of *trans* lactone **12** (prepared from racemic **1**) in the presence of the CSA exhibited two doublets of equal area (1.0–1.1 ppm) for this methyl group while the sample **12**, prepared as described above from optically pure **1**, showed *only* the upfield doublet.[21] If the Pirkle model[20] is assumed for the complex between lactone **12** and the CSA, then the upfield position of the doublet suggests that the 5-methyl group and the anthryl (shielding) group are on the same side of the complex. This reasoning is consistent with the absolute configuration indicated for **12** and for adduct **10**. These results confirm that the face selectivity in the photoaddition step was complete and that the methodology described herein is effective for the preparation of substrates of known absolute configuration and of high optical purity.

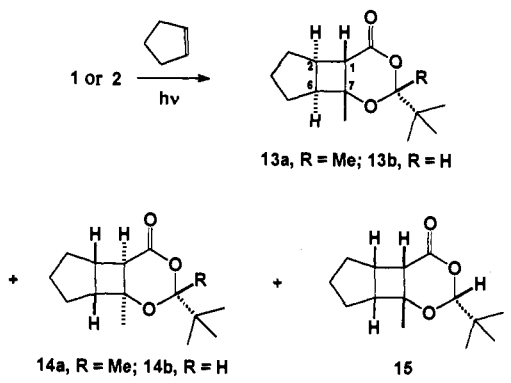
(18) (a) Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Am. Chem. Soc.* **1979**, *101*, 6116. (b) Robson, R.; Grubb, P. W.; Barltrop, J. A. *J. Chem. Soc.* **1964**, 2153.

(19) Lange, G. L.; Organ, M. G. *Synlett* **1991**, 665.

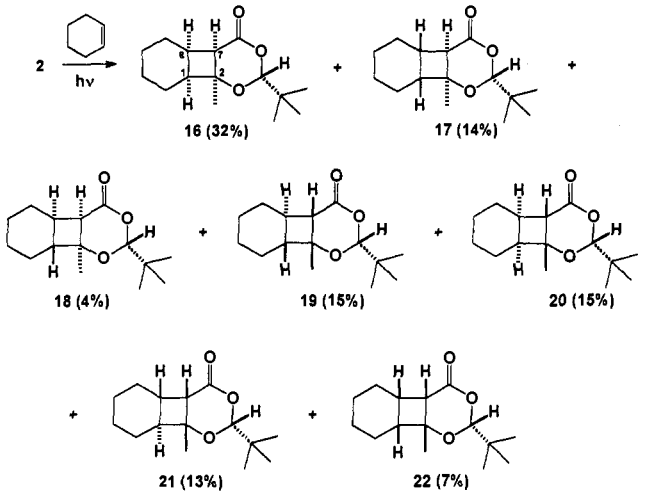
(20) Pirkle, W. H.; Hoover, D. J. In *Topics in Stereochemistry*; Allinger, N. L., Eliel, E.L., Wilen, S. H., Eds.; Wiley-Interscience: New York, 1982; Vol. 13, p 263.

(21) In an additional ^1H NMR analysis, the 5-Me resonance was decoupled by irradiation of the H-5 signal at ~4.5 ppm and only one singlet was observed in the optically active sample of **12**.

Scheme 4



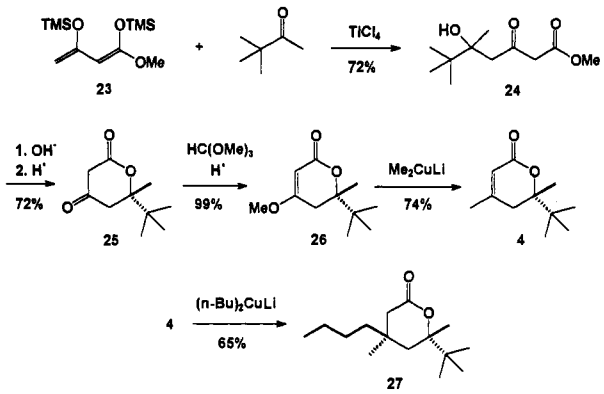
Scheme 5



In the third photoaddition of this series, **1** and cyclopentene gave a mixture of *anti* adducts **13a** (90%) and **14a** (9%) (Scheme 4) with yields based on recovered **1**. A sample of deuterated **1** (2-CD_3) was irradiated along with cyclopentene also, and the ^1H NMR spectra of the adducts were compared to distinguish between the 7- and 9-methyl groups in each. The chemical shift of the 9-methyl resonance in these adducts is of diagnostic value. In the minor adduct **14a**, in which the cyclopentene has added to the top face of **1**, the 9-methyl resonance is significantly deshielded and appears at 1.78 ppm, while in **13a**, formed by addition to the bottom face of **1**, this methyl signal is at 1.41. This same deshielding effect of the small axial group on C-9 will be used later in assigning the face selectivity of adducts derived from **2**. The H-1/H-2 coupling constants of 5.6 and 4.4 Hz for **13a** and **14a**, respectively, were consistent with the assigned *anti* stereochemistries. Thus, in these three irradiations of **1**, cyclohexene and the ethylene ketal of cyclohexenone added *exclusively* to the bottom face (the same side as the *tert*-butyl group) while the smaller cyclopentene added primarily to the bottom face (ratio 10:1).

Reactions of 2. As mentioned in the Introduction, Seebach found that conjugate addition or hydrogenation reactions took place exclusively on the top face of **2**.[3] Photoaddition of **2** with cyclohexene was reported,[7] but the structures of the adducts were not elucidated. Herein we report an investigation of the photoaddition of **2** with both cyclohexene and cyclopentene, so that the diastereoselectivity may be compared with that of dioxinone **1**. Irradiation of **2** and cyclohexene in 20% acetone/acetonitrile gave seven adducts (Scheme 5) in a combined yield of 93%. The adducts were separated by flash chromatography, but because of the complex mixture obtained, it was necessary to analyze some samples which contained minor amounts of other components. In making the structural assignments, decoupling

Scheme 6



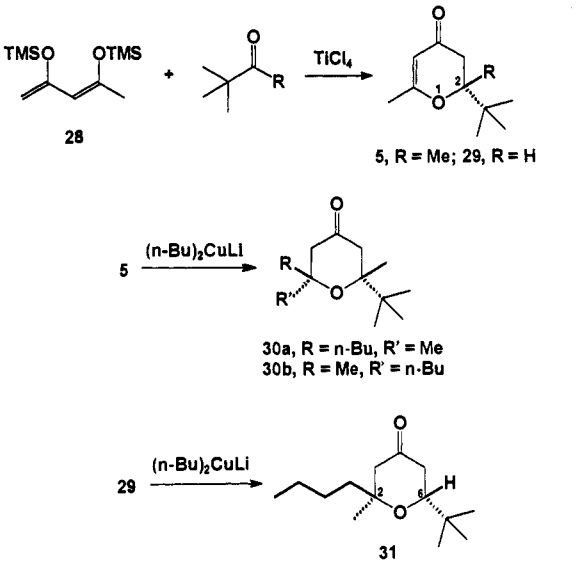
experiments and comparison of the ^{1}H NMR spectra with those of the adducts derived from **1** were invaluable. The ^{1}H NMR chemical shift of the acetal proton (H-4) in the adducts appears diagnostic for the face selectivity of the cycloadditions. An H-4 resonance in the region 4.7–5.0 ppm is indicative of an adduct in which cyclohexene has added from the bottom face of **1** while a resonance in the region 5.2–5.6 ppm indicates addition from the top face. A related example supporting this conclusion has been reported,[6] and another example will be described in the next paragraph. The percentage composition of the adducts was determined by measuring the relative areas of the acetal protons (4.7–5.6 ppm) in the ^{1}H NMR spectrum of the mixture. The three less polar adducts from the chromatographic separation **16** (32% of adduct mixture), **17** (14%), and **18** (4%) were formed by addition of cyclohexene to the top face of **2**, while the more polar adducts **19** (15%), **20** (15%), **21** (7%), and **22** (13%) were formed by addition on the bottom face. The product distribution indicates there was no facial selectivity with 50% photoaddition occurring from the top face and 50% from the bottom face of **2**.

Photoaddition of **2** and cyclopentene gave three adducts (Scheme 4) in a combined yield of 53% (not maximized). Addition of cyclopentene from the top face gave the less polar adduct **14b** (55% of product mixture) while addition from the bottom face gave the more polar adducts **13b** (24%) and **15** (21%). The chemical shift of H-9 (the acetal hydrogen) in the ^{1}H NMR spectra was again very useful in determining the facial selectivity of the reaction. This proton appeared at 5.42 ppm in **14b** and at 4.87 and 4.75 ppm in **13b** and **15**, respectively. The H-1/H-2 coupling constants of 5.6 Hz for the *anti* adducts **13b** and **14b** and 10.6 Hz for the *syn* adduct **15** were as expected. An NOE difference experiment with **14b** (Figure 1) confirmed the stereochemistry assigned to this adduct. For example, irradiation of H-9 resulted in enhancement of the signals for H-2 and H-6 while irradiation of the *tert*-butyl group enhanced the signals for H-1 and the 7-methyl group. This photoaddition actually resulted in more reaction on the top face (55%) of **2** than on the bottom face (24 + 21 = 45%).

After discovering the impressive diastereoselectivity achieved with **1** (and comparing it with **2**), we felt it would be of interest to examine the selectivity of related heterocycles in which each of the ring oxygen atoms was replaced by a methylene group while the remainder of the carbon skeleton was identical. In the next two sections, the preparation and ground-state reactions of the α,β-unsaturated δ-lactone **4** (the oxygen at the 1-position of **1** is replaced by a methylene group) and the 2,3-dihydro-4*H*-pyran-4-one **5** (the 3-oxygen is replaced by a methylene) are presented. We then describe crystallographic data and theoretical predictions which are used to explain the diastereoselectivities observed with the three heterocycles.

Preparation and Reactions of 4. Lactone **4** was prepared as outlined in Scheme 6. Condensation of the bis-trimethylsilyl

Scheme 7



ether of methyl acetoacetate (**23**)[22] with pinacolone using Chan methodology[23] gave **24**, which was lactonized[24] to give **25**. Enol ether formation gave **26**, which upon reaction with Me_2CuLi in the presence of trimethylsilyl chloride followed by elimination of methoxide gave the desired substrate **4**.

To investigate the diastereoselectivity of **4**, it was treated with $(n\text{-Bu})_2CuLi$ to give **27** in 65% yield. Examination of the ^{1}H and ^{13}C NMR spectra of the product revealed the presence of only one isomer. The stereochemistry of **27** was determined by NOE difference experiments. These results indicated that the cuprate reagent attacked the top face of **4** exclusively, the same facial selectivity that was observed with dioxinone **1**. Numerous other examples of high diastereoselectivities in addition reactions (catalytic hydrogenations[25] or cuprate additions[26]) to δ-substituted α,β-unsaturated δ-lactones have been reported. In all examples, the *trans* product was the exclusive or major isomer formed, i.e. the same stereochemistry as observed in our reactions of **4**.

Preparation and Reactions of 5 and 29. Dihydropyranone **5** was prepared by reaction of the bis-trimethylsilyl ether of 2,4-pentanedione (**28**) and pinacolone in the presence of $TiCl_4$[27] (Scheme 7). **29** was prepared similarly using **28** and pivaldehyde. The hetero-Diels–Alder reaction has also been used in the preparation of dihydropyranones.[28] Reaction of **5** with $(n\text{-Bu})_2CuLi$ gave a 50:50 mixture of stereoisomers **30a** and **30b**. On the other hand, cuprate addition to **29** gave only one diastereomer, **31**, as judged by ^{1}H NMR spectrometry of the crude mixture and purified product. The stereochemistry of this isomer was established by NOE difference experiments. For example, irradiation of the *tert*-butyl group of **31** resulted in enhancement of the 2-methyl resonance while irradiation of H-6 enhanced the

(22) (a) Yamamoto, K.; Suzuki, S.; Tsuji, J. *Chem. Lett.* **1978**, 649. (b) Gilbert, J.C.; Kelly, T. A. *Tetrahedron* **1988**, *44*, 7587. (c) Molander, G. A.; Cameron, K.O. *J. Am. Chem. Soc.* **1993**, *115*, 830.

(23) Chan, T.-H.; Brownbridge, P. *J. Chem. Soc., Chem. Commun.* **1979**, 578.

(24) Peterson, J. R.; Winter, T. J.; Miller, C. P. *Synth. Commun.* **1988**, *18*, 949.

(25) (a) Pilli, R. A.; Murta, M. M. *J. Org. Chem.* **1993**, *58*, 338. (b) Danishefsky, S.; Kato, N.; Askin, D.; Kerwin, J. F., Jr. *J. Am. Chem. Soc.* **1982**, *104*, 360.

(26) (a) Takano, S.; Shimazaki, Y.; Moriya, M.; Ogasawara, K. *Chem. Lett.* **1990**, 1177. (b) Bartmann, W.; Beck, G.; Granzer, E.; Jendralla, H.; v. Kerekjarto, B.; Wess, G. *Tetrahedron Lett.* **1986**, *27*, 4709. (c) Marshall, J. A.; Andrews, R.C. *Tetrahedron Lett.* **1986**, *27*, 5197. (d) Marshall, J. A.; Coghlan, M. J.; Watanabe, M. *J. Org. Chem.* **1984**, *49*, 747. (e) Pirkle, W. H.; Adams, P. E. *J. Org. Chem.* **1980**, *45*, 4117.

(27) Peterson, J. R.; Kirchhoff, E. W. *Synlett* **1990**, 394.

(28) (a) Myles, D. C.; Danishefsky, S. J.; Schulte, G. *J. Org. Chem.* **1990**, *55*, 1636 and references therein. (b) Spero, D. M.; Adams, J. *Tetrahedron Lett.* **1992**, *33*, 1143. (c) Annunziata, R.; Cinquini, M.; Cozzi, F.; Cozzi, P. G.; Raimondi, L. *J. Org. Chem.* **1992**, *57*, 3605.

Table 1. Comparison of the Degree of Pyramidalization in 1,3-Dioxinones, α,β-Unsaturated δ-Lactones, Dihydropyranones, and 2-Cyclohexenones[a]

						pyramidalization[b] (deg)			
R_1	R_2	R_3	R_4	X_1	X_3	C_4=O	C_5	C_6	ref[c]
					Dioxinones				
H	H	H	H	O	O	9.16 (b)	6.99 (b)	7.89 (b)	*ab initio* SCF
H	H	H	H	O	O	13.59 (b)	11.29 (b)	11.71 (b)	*ab initio* MP2
Me	H		spiro-C_9H_{18}	O	O	9.24 (b)	5.26 (a)	7.41 (b)	farbef
Me	H		spiro-$C_7H_8O_3$	O	O	8.46 (b)	8.07 (b)	7.44 (b)	fenhel
Me	Br	H	*tert*-butyl	O	O	12.57 (b)	10.31 (b)	11.85 (b)	Seebach, ref 3[d]
Me	H	Me	*tert*-butyl	O	O	6.86 (b)	0.94 (b)	5.89 (b)	**1**, this study[e]
					α,β-Unsaturated δ-Lactones				
H	H	H	H	C	O	9.99 (b)	4.04 (b)	4.55 (b)	*ab initio* SCF
H	H	H	H	C	O	13.91 (b)	5.64 (b)	5.99 (b)	*ab initio* MP2
H	H	H	$C_{15}H_{21}O_8$	C	O	8.15 (b)	3.17 (b)	5.48 (a)	anamar[e]
Me	Me	H	$C_{21}H_{33}O_3$	C	O	10.78 (b)	2.91 (a)	8.15 (b)	berjen
H	Me	H	$C_{24}H_{33}O_2$	C	O	9.34 (b)	2.82 (b)	1.69 (b)	cajcof
Me	H	H	$C_{11}H_7O_2$	C	O	13.96 (b)	5.03 (b)	6.85 (b)	sejnok
Me	H	H	$C_{10}H_{17}O_3$	C	O	11.94 (b)	6.54 (b)	5.00 (b)	sejpay
H	H	H	$C_{10}H_{11}O_3$	C	O	11.55 (b)	6.05 (b)	4.15 (b)	vocsov
					Dihydropyranones				
H	H	H	H	O	C	1.12 (a)	3.16 (b)	4.86 (b)	*ab initio* SCF
H	H	H	H	O	C	0.48 (b)	5.32 (b)	7.25 (b)	*ab initio* MP2
H	H	H	$C_8H_{13}O_4$	O	C	1.75 (b)	10.83 (a)	0.02 (b)	vabrul[e]
H	Me	H	$C_9H_{15}O_2$	O	C	3.38 (b)	5.17 (b)		bukpay[f]
H	Me	H	$C_{11}H_{17}O_5$	O	C	3.24 (a)	1.50 (b)	4.31 (b)	dijcii
C_5H_9O	Me	H	Me	O	C	1.02 (a)	3.44 (b)	4.50 (b)	bamhec
					2-Cyclohexenones				
H	H	H	H	C	C	2.60 (a)	0.79 (b)	1.86 (b)	*ab initio* SCF
H	H	H	H	C	C	2.08 (a)	0.76 (b)	2.28 (b)	*ab initio* MP2
H	H	C_6H_5	C_6H_5	C	C	1.67 (a)	2.05 (b)	3.08 (b)	seczuv
H	H	C_6H_5	C_6H_5	C	C	1.27 (a)	1.07 (a)	0.33 (a)	seczop
H	H	H	C_3H_5	C	C	2.14 (b)	0.03 (a)	0.99 (a)	secpar
H	Me		spiro-$C_8H_{15}Br$	C	C	0.85 (b)	0.40 (b)		vilkac[f]
H	Me	H	C_5H_8	C	C	1.20 (a)	3.53 (b)	10.44 (b)	tridko[e]

[a] In Figure 3 the positions of R_1–R_4 and X_1 and X_3 are shown and the degree of pyramidalization at C-4 (for example) is defined as the angle θ between the line C_4–O_9 and the plane C_4–C_5–C_6. The substituent may be below the plane (b) or above the plane (a), where above the plane refers to the direction of ring pucker at C-2. *Ab initio* calculations are based on full geometry optimizations on the unsubstituted system at the MP2 (frozen core) and SCF levels of theory using the 6-31G* basis set. [b] Δ values (ref 32) for *ab initio* (MP2) dioxinone are (Å) as follows: C_4, 0.039; C_5, 0.084; C_6, 0.001. For the crystal **1**: C_4, 0.020; C_5, 0.000; C_6, 0.000. [c] The reference codes for the crystal structures were taken from the Cambridge Crystallographic Database. [d] Crystallized with two independent molecules in the unit cell. Pyramidalization numbers are similar for both forms. [e] Limitations of the X-ray data for the protons may have led to inaccurate values for the locations of the H atoms. [f] No data were given for the hydrogen atoms.

signal for the first methylene group of the *n*-butyl substituent at C-2. These results demonstrate that, in cuprate additions to **5**, the additional steric hindrance on the top face provided by the 2-methyl group dramatically reduces the diastereoselectivity compared with that of **29**. Other investigations of cuprate additions to dihydropyranones have been described,[29] and in general, the diastereoselectivities are not as high as those observed with the dioxinones or the unsaturated δ-lactones. But the results are more ambiguous, as some of the studies used conformationally restricted bicyclic substrates and, in others, solvent or reagent dependency was noted.[29]

Crystallographic Analyses and Theoretical Predictions. The substrates **1**, **4**, and **5** have the same skeletons but differ in the number and position of oxygen atoms in each heterocycle. The diastereoselectivity for each substrate upon reaction with cuprate reagents was described in earlier sections. With **1** and **4**, the addition took place exclusively on the top face while with **5** a 50:50 mixture of stereoisomers was obtained. We wished to determine if high-level theoretical predictions of the geometries of these substrates in the ground state might provide some rationale for the selectivities observed. Seebach suggested[3] that pyramidalization of the enone portion of **2** (C-4 to C-6) "is not causing stereoselectivity, but that both phenomena have the same origin." Thus, we were particularly interested in comparing that aspect of the geometries of **1**, **4**, and **5**.

In Table 1, the degrees of pyramidalization predicted theoretically or determined by analysis of X-ray data for a number of heterocycles related to **1**, **4**, **5**, and 2-cyclohexenone (**32**) are presented. The *ab initio* SCF/6-31G* and MP2/6-31G* predictions were made on the unsubstituted heterocycles while the X-ray crystal structures[30] were extracted from the 1992 release of the Cambridge Crystallographic Database.[31] Reference codes from the database for each structure are included in Table 1. In addition, we were successful in obtaining an X-ray structure determination of our most important substrate, dioxinone **1** (Figure 2, Table 1). The extent of pyramidalization must be carefully defined. We measure it relative to a plane formed by the formally sp^2 hybridized atoms C-4, C-5, and C-6 with the substituents attached to those atoms being above (a) or below (b) the plane by an angle θ (Figure 3). An alternative method of measuring pyramidalization (Δ values) has been described,[32] but these values do not convey as effectively the extent of pyramidalization present in the enone portion of the ring. A few Δ values are listed in footnote 1 of Table 1 for comparison. To facilitate comparison of these four types of substrates, numbering of the ring atoms as in dioxinone (Figure 3) is maintained throughout this discussion. In general, the MP2 calculations predict a greater degree of pyramidalization at C-4 to C-6 than the SCF values for each of the four systems (Table 1) and the agreement between the theory and the values derived from the crystal structures is encouraging. Figures 4 and 5 summarize

(29) Goodwin, T. E.; Rothman, N. M.; Salazar, K. L.; Sorrels, S. L.; Evans, F. E. *J. Org. Chem.* **1992**, *57*, 2469 and references therein.

(30) Only structures similar to the heterocycles of interest are included, and compounds with additional conjugated double bonds or with rings fused to the parent ring are excluded.

(31) Allen, F. H.; Kennard, O.; Taylor, R. *Acc. Chem. Res.* **1983**, *16*, 146.

(32) Dunitz, J. D. *X-Ray Analysis and the Structure of Organic Molecules*; Cornell University Press: Ithaca, NY, 1979; pp 368–369.

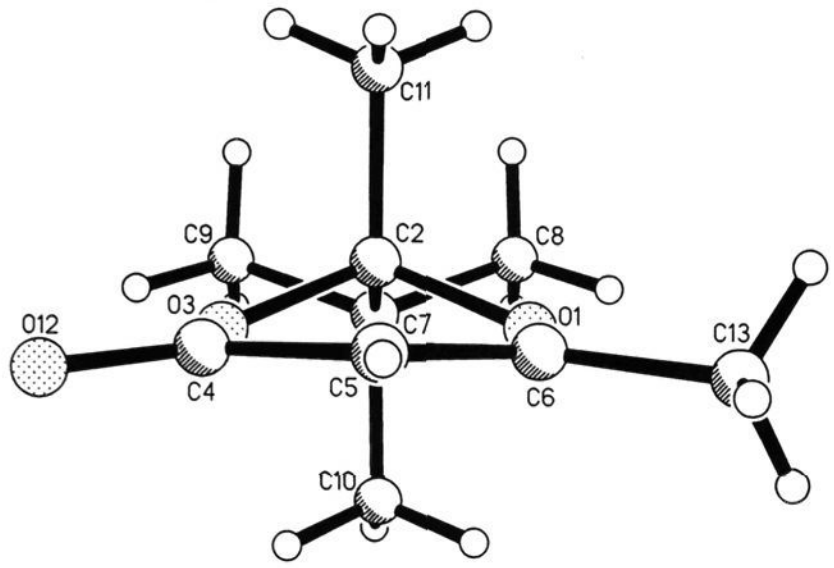


Figure 2. Ball and stick diagram representing the structure of **1** as determined by X-ray diffraction analysis.

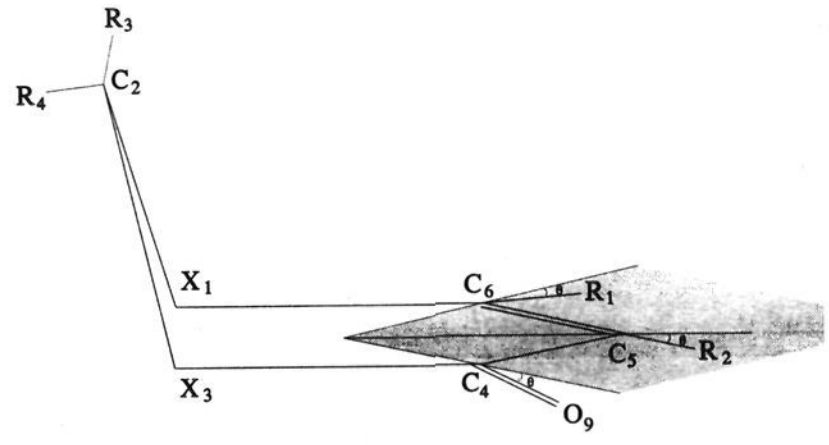


Figure 3. Measure of pyramidalization employed in this work involving the angle θ between the line (for example, C_4–O_9) and the plane formed by C_4–C_5–C_6.

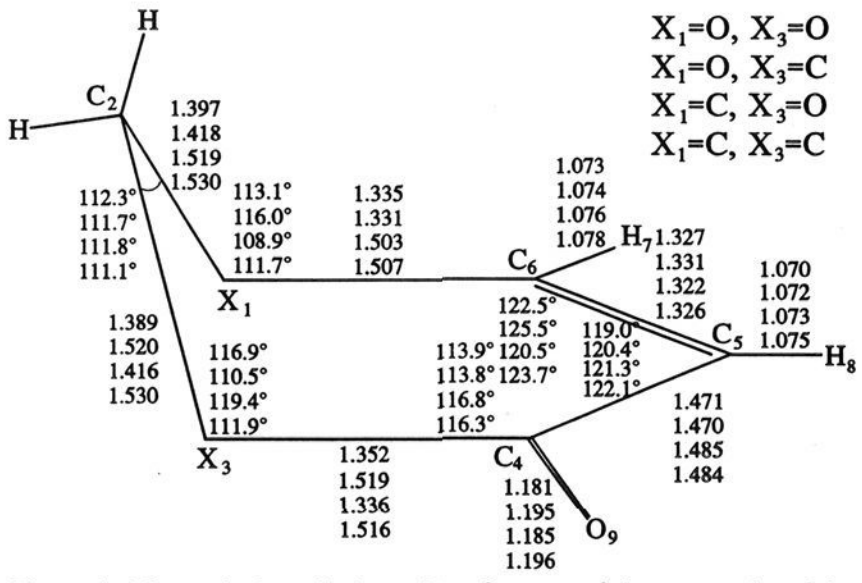


Figure 4. Theoretical predictions of key features of the geometries of the four unsubstituted compounds: dioxinone (X_1 = O, X_3 = O), dihydropyranone (X_1 = O, X_3 = C), lactone (X_1 = C, X_3 = O), and cyclohexenone (X_1 = C, X_3 = C). The *ab initio* predictions were made at the Hartree–Fock level using the 6-31G* basis set.

the important bond angles and bond lengths determined by the two theoretical methods for the four unsubstituted substrates: 1,3-dioxinone (X_1 = X_3 = O), α,β-unsaturated δ-lactone (X_1 = CH_2, X_3 = O), dihydropyranone (X_1 = O, X_3 = CH_2), and 2-cyclohexenone (X_1 = X_3 = CH_2). As expected, bonds lengthen with the MP2 method as compared to the SCF level of theory. The one exception is the C-4–C-5 bond, which has shortened slightly to 1.467 Å (MP2) from 1.471 Å (SCF) in the dioxinone. It is expected that, upon the inclusion of electron correlation (MP2), an important additional contribution to the wave function would be from excitation into the LUMO, which in this case is mainly a π^* orbital. This π^* orbital has nodes in the C-5–C-6 and C-4–O-9 bonds but a bonding interaction between C-4 and C-5.

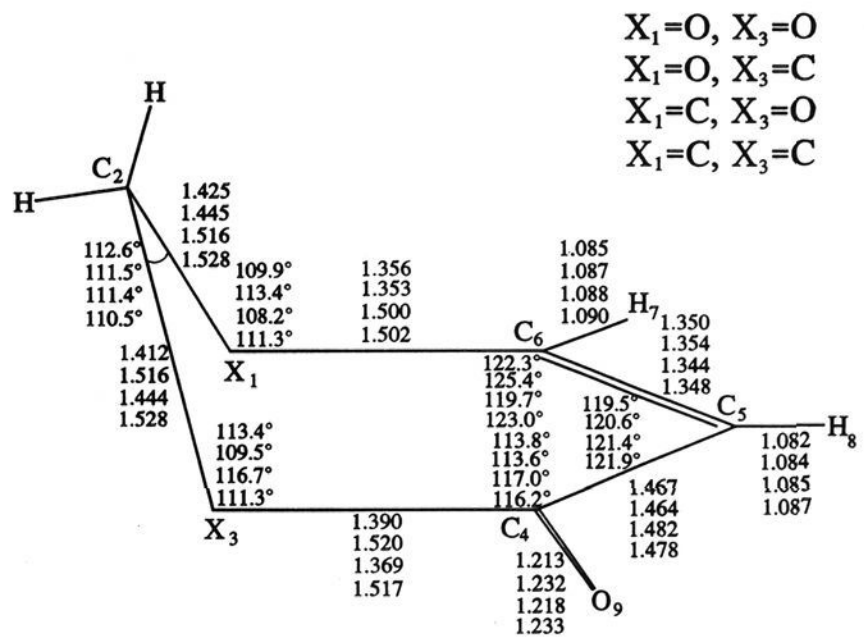


Figure 5. Theoretical predictions of key features of the geometries of the four unsubstituted compounds: dioxinone (X_1 = O, X_3 = O), dihydropyranone (X_1 = O, X_3 = C), lactone (X_1 = C, X_3 = O), and cyclohexenone (X_1 = C, X_3 = C). The *ab initio* predictions were made using Møller–Plesset perturbation theory to second order (MP2) with the 6-31G* basis set.

Table 2. Comparison of Internal Bond Angles and Bond Lengths in Various Dioxinone Compounds[a]

	theoretical		crystallographic data			
	SCF	MP2	farbef	fenhel	**2** (5-Br)	**1**
			Internal Angles			
O_1	113.1	109.9	116.2	114.3	113.5	117.2
C_2	112.3	112.6	110.1	111.4	109.1	111.6
O_3	116.9	113.4	117.8	116.4	115.2	119.4
C_4	113.9	113.8	115.2	115.3	113.3	116.0
C_5	119.0	119.5	121.4	120.6	121.8	120.3
C_6	122.5	122.3	120.8	121.4	118.9	121.7
			Bond Lengths			
O_1—C_2	1.40	1.43	1.43	1.43	1.43	1.43
C_2—O_3	1.39	1.41	1.45	1.42	1.43	1.43
O_3—C_4	1.35	1.39	1.39	1.38	1.36	1.37
C_4—C_5	1.47	1.47	1.44	1.44	1.46	1.44
C_5—C_6	1.33	1.35	1.33	1.33	1.33	1.33
C_6—O	1.34	1.36	1.36	1.37	1.35	1.36
C_4=O_9	1.18	1.21	1.21	1.21	1.19	1.22

[a] The structures of the molecules and their crystallographic reference codes are given in the same order as the first six entries in Table 1. Theoretical predictions are made at the SCF and MP2 levels using the 6-31G* basis set.

Table 2 presents a comparison of bond lengths and angles for various dioxinone species. Four different crystal structures (including our own) and the two theoretical methods are presented. The general agreement between the highest level predictions (MP2) and experiment is quite good. The largest deviation between theory and experiment for any of the ring bond lengths or the carbonyl distance is less than 0.03 Å or ca. 3%. Two possible exceptions to this very good agreement are the bond angles at the ring oxygens. MP2 theory predicts them to be 7.3° (O-1) and 6.0° (O-3) smaller than in our crystal structure. Complete geometry optimizations at the semiempirical MNDO level of theory of the unsubstituted and the fully substituted dioxinone **1** indicated that upon substitution, the oxygen bond angles increase by 2.7° (O-1) and 1.9° (O-3). Thus, the effects of substituents partially explain the smaller angles obtained theoretically. In addition, bond angles about oxygen atoms in rings frequently are smaller with the MP2 method as compared to the SCF level of theory.[33]

A definite trend is observed for the degree of pyramidalization in the four heterocycles of interest (Table 1): 1,3-dioxinones >

(33) For example, in butyrolactone and valerolactone, the COC angles decrease by 2.2° and 2.1° on going from HF/6-31G* to MP2/6-31G*. Wiberg, K. B.; Waldron, R. F. *J. Am. Chem. Soc.* **1991**, *113*, 7697.

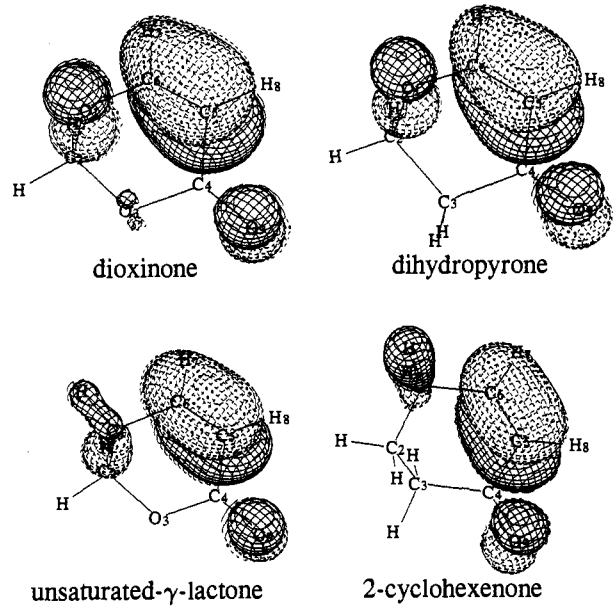


Figure 6. Orbital contour plots of the highest occupied molecular orbital (MO 26, π) in the four unsubstituted systems. The orbitals are taken from an SCF calculation using the 6-31G* basis set.

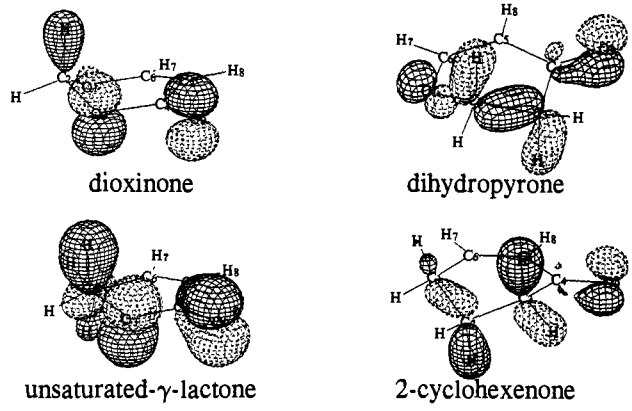


Figure 7. Orbital contour plots of molecular orbital 24 in the four unsubstituted systems. The orbitals are taken from an SCF calculation using the 6-31G* basis set.

α,β-unsaturated δ-lactones > dihydropyranones > 2-cyclohexenones. In those systems where there is a significant pyramidalization, the groups at C-4 to C-6 are always bent below the plane, i.e., away from the pucker at C-2. Pyramidalization of the carbonyl oxygen at C-4 is especially pronounced when an oxygen atom is present at the 3-position, as in the dioxinones and δ-lactones.

Why do compounds such as the dioxinones possess such significant pyramidalization in the enone portion of the molecule? The molecular orbitals of this system were analyzed to gain some insight into this feature. Studying the higher occupied orbitals often can help rationalize the geometry of a molecule. Occupied orbitals 26 (HOMO) and 24 for the four systems are depicted in Figures 6 and 7. The HOMO (26) is a π-type orbital across the C-5–C-6 double bond. As Figure 6 indicates, dioxinones and dihydropyranones possess oxygens next to the double bond and the p-type orbital on the oxygen has an out-of-phase interaction with the π cloud. This effect could be the cause of a torque on C=C, leading to slight pyramidalization of substituents attached to C-5 and C-6. The pyramidalization would likely be small due to the large contribution of the π system to this molecular orbital, which would tend to maintain planarity. An effect is seen in molecular orbital 24 when the substrates possess an oxygen at the 3-position, as displayed in dioxinones and lactones (Figure 7). A strong out-of-phase interaction between the p-type orbitals on O-3 and the carbonyl oxygen is evident and would lead to pyramidalization of the C=O. It appears that an oxygen at the 1- or 3-position leads to pyramidalization of that side of the ring, with a larger effect when substrates possess an oxygen at the 3-position. The other high-lying occupied molecular orbital 25, which is not shown here, is an n orbital, a lone pair orbital on the carbonyl oxygen. When electron correlation is included, the additional out-of-phase interaction of the p-orbital on the carbonyl with the π^* orbital across C-4–C-5 would likely lead to greater pyramidalization of the carbonyl when compared to the case of the SCF level. This particular molecular orbital looks very similar in all four systems studied. The two highest occupied orbitals (25 and 26) closely resemble the highest occupied orbitals in the acrolein system.[34] The nonplanarity of double bonds and its relationship to diastereoselectivity in reactions has been studied in some detail previously.[35-40] Several possible explanations were given for the observed facial selectivities based on computations on model systems. All such studies place some emphasis on the out-of-plane bending of the double bond but differ in their rationalization of the exact causes of such a distortion.

Summary and Conclusions

This study has been concerned particularly with the reactions and geometries of three heterocycles: dioxinone **1**, unsaturated lactone **4**, and dihydropyranone **5**. These substrates differ in the number or location of oxygen atoms present in the ring, but all have identically positioned alkyl groups and double bonds relative to the carbonyl group. The same cuprate reagent, $(n\text{-Bu})_2\text{CuLi}$, has been used in reactions with each substrate although other ground- and excited-state reactions have also been investigated. Reactions of **1** and **4** with the butyl cuprate reagent resulted in exclusive attack from the top face (side opposite the *tert*-butyl group) while reaction with **5** showed no selectivity and a 50:50 mixture of isomers was obtained. Theoretical predictions of the geometries of the three unsubstituted heterocycles showed the pyramidalization of the enone portion of the substrates. This pyramidalization was of special interest, as Seebach had suggested[3] that distortion from planarity of this moiety was related to the selectivity observed in reactions with dioxinone **2**. The trends observed from these theoretical predictions are supported by the X-ray structures obtained from the Cambridge Crystallographic Database for each type of heterocycle (Table 1). During this investigation, we determined the structure of dioxinone **1** by X-ray crystallography. Figure 2 clearly shows pyramidalization of the enone system, the sofa conformation of the ring, and the axial orientation of the 2-methyl group in **1**. The theoretical predictions and the X-ray structures indicate that the degree of pyramidalization decreases in the following order: dioxinone > α,β-unsaturated δ-lactone > dihydropyranone > 2-cyclohexenone. The magnitude of pyramidalization of the dioxinone system of approximately 11° to 14° (MP2) is notably greater than previously suggested[3] and also significantly larger than predicted in some

(34) Jorgensen, W. L.; Salem, L. *The Organic Chemist's Book of Orbitals*; Academic Press: New York, 1973; p 181.
(35) Burdisso, M.; Gamba, A.; Gandolfi, R.; Toma, L.; Rastelli, A.; Schiatti, E. *J. Org. Chem.* **1990**, *55*, 3311.
(36) (a) Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438. (b) Paddon-Row, M. N.; Rondan, N. G.; Houk, K.N. *J. Am. Chem. Soc.* **1982**, *104*, 7162. (c) Houk, K. N.; Rondan, N. G.; Brown, F. K. *Isr. J. Chem.* **1983**, *23*, 3. (d) Houk, K. N.; Rondan, N. G.; Brown, F. K.; Jorgensen, W.L.; Madura, J. D.; Spellmeyer, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 5980. (e) Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Mareda, J.; Mueller, P.H.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 4974. (f) Houk, K. N. *Pure Appl. Chem.* **1983**, *55*, 277.
(37) (a) Kahn, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650. (b) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 663.
(38) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.
(39) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, *98*, 4054.
(40) (a) Huang, X. L.; Dannenberg, J. J.; Duran, M.; Bertrán, J. *J. Am. Chem. Soc.* **1993**, *115*, 4024. (b) Huang, X. L.; Dannenberg, J. J. *J. Am. Chem. Soc.* **1993**, *115*, 6017.

other systems containing sp^2 centers.[35] The face selectivity studies we have reported for the first three substrates with the cuprate reagent display essentially the same trend as the degree of pyramidalization. Thus we suggest that any attempt to rationalize these face selectivities obtained in the ground-state reactions with these compounds should give serious consideration to the extent of pyramidalization of the enone moiety in these substrates. Due to this pyramidalization, the carbon atoms in the enone system could be viewed as having hybridization somewhat intermediate between sp^2 and sp^3 and thus are already displaced along the reaction coordinate toward the tetrahedral configuration of the transition state and product. Attack from the bottom face also would require the additional energy for the substituents to invert through a planar sp^2 configuration.

Clearly, other factors such as steric hindrance are also involved in determining the selectivities observed with these classes of compounds. For example, dihydropyranone **26** undergoes cuprate addition exclusively from the top face, but **5**, with an axial 2-methyl group rather than a hydrogen atom, yields a 50:50 mixture of isomers. On the other hand, the presence of the 2-methyl group in dioxinone **1** still results in exclusive attack of cuprate reagents on the top face because of the greater degree of pyramidalization of this heterocycle.

The photochemical studies reported here are more limited in scope but reveal a remarkable reversal of facial selectivity compared with the cases of the cuprate additions. Cycloaddition of **1** and cyclohexene or the related ketal yielded adducts formed by exclusive attack on the *bottom* face. But with **2**, which has only an axial hydrogen at C-2 rather than a methyl group, a 50:50 mixture is obtained. A steric effect is clearly responsible for this difference. The size of the alkene is also a factor in these reactions. Photoaddition of **1** with cyclohexene or the corresponding ketal takes place exclusively on the bottom face while reaction with the smaller cyclopentene shows a 9:1 preference. In this report we offer no additional insight to account for the fact that the photoadditions generally take place from the face opposite to that for the ground-state reactions. Seebach has suggested that reverse pyramidalization in the triplet state of the dioxinone may be responsible[3] while Sato proposes that the dioxinone may react from different conformations which are dependent on the type of reaction involved.[6]

One of the ultimate objectives of these investigations was to develop methodology for the synthesis of optically active products by asymmetric induction. We described a study in which adduct **10** was prepared from optically active **1** (R = CD_3),[10] which in turn had been prepared from the readily available (*R*)-3-hydroxybutyric acid.[9] The conversion of **10** to the optically pure lactone **12** after loss of the chiral auxiliary established the viability of the induction methodology.

Experimental Section

General Methods. ^1H and ^{13}C NMR spectra were recorded on a 200-MHz Varian Gemini or a 400-MHz Varian Unity spectrometer with $CDCl_3$ as solvent and TMS as internal standard. The multiplicities of the ^{13}C resonances were determined by the attached proton test (APT), which gave positive (+) quaternary C and CH_2 signals and negative (–) CH and CH_3 signals, or by DEPT experiments. IR spectra were recorded on a Nicolet Model 20 SX/C FTIR spectrophotometer in CCl_4 solution using NaCl cells, and mass spectra were obtained on a Krakos MS 890 spectrometer. Products were purified by medium-pressure liquid chromatography (MPLC) using 230–400 mesh silica gel. A solvent mixture of EtOAc and hexanes was chosen which gave the product of interest an R_f of 0.35 on thin-layer chromatography (TLC). TLC analyses were performed on silica gel GF 254 plates with a thickness of 0.25 mm. Melting points are uncorrected.

Solvents were prepared as follows: ether and THF were distilled from CaH_2 and then from sodium/benzophone ketyl; CH_2Cl_2 was distilled from CaH_2; and toluene was distilled from sodium. Reactions sensitive to air or moisture were conducted in flame-dried flasks under an atmosphere of argon.

General Procedure for *n*-Butyl Cuprate Additions to Enone Systems. To a flame-dried round-bottomed flask was added CuI (3*n* mmol) and dry ether (4 mL) under argon. The stirred suspension was cooled to 0 °C, and *n*-butyllithium (6*n* mmol, 1.6 M in hexanes) was added over 20 min. The cuprate solution was further cooled to –78 °C, and the enone (*n* mmol) in dry ether (2 mL) was added dropwise by cannula. The reaction was allowed to warm to –20 °C over 2 h, a 1:1 NH_3/NH_4Cl saturated solution (12 mL) was added, and the mixture was stirred in air until a dark-blue color persisted. The aqueous phase was separated and extracted with ether (3×). The combined organic phases were washed with brine and dried (anhydrous $MgSO_4$). The solvent was removed *in vacuo*, and the resultant oil was separated by MPLC.

6β-*n*-Butyl-2α-*tert*-butyl-2β,6α-dimethyl-1,3-dioxan-4-one (6a). Following the general cuprate procedure, CuI (619 mg, 3.25 mmol) and *n*-butyllithium solution (4.06 mL, 6.50 mmol) were reacted and the resultant cuprate was mixed with dioxinone **1** (200 mg, 1.08 mmol). Purification of the crude product by MPLC (5% EtOAc/hexanes) gave **6a** (191 mg, 73%) as a clear oil: ^1H NMR ($CDCl_3$) δ 2.74 (d, *J* = 16.5 Hz, 1H, H-5β), 2.46 (d, *J* = 16.5 Hz, 1H, H-5α), 1.62–1.56 (m, 2H, H-1′), 1.49 (s, 3H, 2-CH_3), 1.29–1.23 (m, 4H, H-2′ and H-3′), 1.21 (s, 3H, 6-CH_3), 0.98 (s, 9H, C(CH_3)$_3$), 0.91 (t, *J* = 6.9 Hz, 3H, 4′-CH_3); ^{13}C NMR ($CDCl_3$) (APT) δ 168.98 (+, C-4), 109.80 (+, C-2), 75.17 (+, C-6), 42.48 (+, C-5), 40.13 (+, *C*(CH$_3$)$_3$), 40.07 (+, C-1′), 27.93 (–, 2-CH_3), 25.70 (+, C-2′), 24.44 (–, C(*C*H$_3$)$_3$), 22.86 (+, C-3′), 22.20 (–, 6-CH_3), 13.92 (–, C-4′); IR (CCl_4) 1755, 1467, 1387, 1323, 1284, 1148 cm^{-1}; EIMS (50 eV) *m/z* (relative intensity) 242 $[M]^+$ (2), 227 $[M - CH_3]^+$ (21), 149 (45), 125 (66), 97 (47), 85 (41), 43 (100).

2α-*tert*-Butyl-6β-ethyl-2β,6α-dimethyl-1,3-dioxan-4-one (6b). To a suspension of CuCN (146 mg, 1.63 mmol) in dry ether (2 mL) at 0 °C under argon was added with stirring over 20 min ethylmagnesium bromide (3.26 mL of a 1.0 M solution in ether, 3.26 mmol). The solution was cooled to –78 °C, a solution of dioxinone **1** (100 mg, 0.54 mmol) in dry ether (1 mL) was added dropwise, and the mixture was allowed to warm to –20 °C over 2 h. The reaction was quenched with a phosphate buffer (5 mL, pH 7), saturated NH_4Cl solution (2 mL) was added, and the mixture was stirred in air until a deep blue color persisted. The aqueous layer was extracted with ether (3×), and the combined organic layers were washed with brine and dried ($MgSO_4$). The solvent was removed, and the residue was purified by flash chromatography (5% EtOAc/hexanes) to give recovered **1** (32 mg) and addition product **6b** (66 mg, 57%, 83% based on recovered **1**): ^1H NMR ($CDCl_3$) δ 2.74 (d, *J* = 17.1 Hz, 1H, H-5β), 2.46 (d, *J* = 17.1 Hz, 1H, H-5α), 1.64 (qd, *J* = 7.6, 3.7 Hz, 2H, CH_3CH_2), 1.49 (s, 3H, 2-CH_3), 1.20 (s, 3H, 6-CH_3), 0.99 (s, 9H, C(CH_3)$_3$), 0.95 (t, *J* = 7.6 Hz, 3H, CH_3CH$_2$); ^{13}C NMR ($CDCl_3$) (APT) δ 169.4 (+, C-4), 110.0 (+, C-2), 75.4 (+, C-6), 40.1 (+, *C*Me$_3$), 39.6 (+, C-5), 35.2 (+, *C*H$_2$CH$_3$), 27.1 (–, 2-CH_3), 24.5 (–, C(*C*H$_3$)$_3$), 24.1 (–, 6-CH_3), 7.5 (–, CH$_2$*C*H$_3$); IR (CCl_4) 1749, 1314, 1285, 1215, 1147 cm^{-1}.

General Procedure for Irradiation of Dioxinones and Cycloalkenes. The quartz irradiation tubes were base-washed and then rinsed with acetone and flame-dried. The appropriate amounts of dioxinone and cycloalkene were placed in an irradiation tube and dissolved in a solvent mixture of 20% acetone/acetonitrile to give an enone concentration of 0.5–2.5 mM. The solutions were deoxygenated with argon (2 min) and the tubes sealed with rubber septa. The irradiations employed a 450-W Hanovia high-pressure mercury vapor lamp which was placed in a water-cooled quartz immersion well. The irradiation tubes were placed in Corex sleeves and strapped to the side of the immersion well, which was then placed in a container of ice/water to maintain a temperature of 0 °C. The reactions were followed by TLC and typically took 8–12 h. At the end of the irradiations the solvent was removed and the crude mixture was separated by flash chromatography.

Irradiation of 1 and Cyclohexene. Using the general conditions, dioxinone **1** (300 mg, 1.63 mmol) and cyclohexene (267 mg, 3.26 mmol, 2 equiv) were dissolved in 20% acetone/acetonitrile (4 mL) and irradiated for 12 h. Separation of the reaction mixture by MPLC (5% EtOAc/hexanes) yielded three crystalline adducts: **7a** (236 mg, 54%), **8** (66 mg, 15%), and **9a** (67 mg, 15%).

4α-*tert*-Butyl-1α,7β,8α-trihydro-2β,4β-dimethyl-3,5-dioxa-6-oxotricyclo-[6.4.0.0^{2,7}]dodecane (7a): mp 108.0–108.5 °C; ^1H NMR ($CDCl_3$) δ 2.69 (d, *J* = 4.4 Hz, 1H, H-7), 2.63 (m, 1H, H-8), 2.43 (m, 1H, H-1), 2.07–1.17 (m, 8H, H's 9, 10, 11, and 12), 1.55 (s, 3H, 2-CH_3), 1.47 (s, 3H, 4-CH_3), 1.03 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (DEPT) 172.29 (quat, C-6), 110.83 (quat, C-4), 77.22 (quat, C-2), 45.63 (CH, C-7), 41.95 (CH, C-1), 39.19 (quat, *C*(CH$_3$)$_3$), 33.48 (CH, C-8), 27.51 (CH_2, C-9), 24.39 (CH_3, C(*C*H$_3$)$_3$), 23.53 (CH_3, 2-*C*H$_3$), 22.02 (CH_2, C-10),

21.99 (CH_3, 4-CH_3), 21.68 (CH_2, C-11), 21.30 (CH_2, C-12); IR (CCl_4) 1732, 1543, 1380, 1310,1261, 1201, 1149, 1105, 1079 cm^{-1}; EIMS (50 eV) *m/z* (relative intensity) 266 $[M]^+$ (0.5), 251 $[M - CH_3]^+$ (1), 209 [M – *tert*-butyl]$^+$ (12), 185 [M – cyclohexane]$^+$ (25), 166 [M – pinacolone]$^+$ (30), 138 [M – (pinacolone + CO)]$^+$ (30), 101 (75), 95 (56), 85 (95), 67 (76), 57 (83), 43 (100). Structure also confirmed by X-ray determination (see supplementary material).

4α-*tert*-Butyl-1β,7β,8β-trihydro-2β,4β-dimethyl-3,5-dioxa-6-oxotricyclo-[6.4.0.0^{2,7}]dodecane (8): mp 89–91 °C; ^1H NMR ($CDCl_3$) δ 2.89 (dd, *J* = 10.2, 2.1 Hz, 1H, H-7), 2.63 (m, 1H, H-8), 2.19 (m, 1H, H-1), 2.00 (m, 2H), 1.65–1.24 (m, 6H), 1.55 (s, 3H, 2-CH_3), 1.44 (s, 3H, 4-CH_3), 1.05 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 171.19 (+, C-6), 109.68 (+, C-4), 74.21 (+, C-2), 46.06 (–, C-7), 43.50 (–, C-1), 39.77 (+, $C(CH_3)_3$), 29.42 (–, C-8), 27.52 (–, 2-CH_3), 24.93 (–, $C(CH_3)_3$), 22.70 (+, C-9), 22.02 (+, C's 10 & 11), 21.95 (–, 4-CH_3), 21.26 (+, C-12); IR (CCl_4) 1738, 1374, 1296, 1249, 1214, 1145, 1119, 1063 cm^{-1}; EIMS (50 eV) *m/z* (relative intensity) 251 $[M - CH_3]^+$ (0.5), 209 [M – *tert*-butyl]$^+$ (4), 185 [M – cyclohexane]$^+$ (15), 166 [M – pinacolone]$^+$ (9), 138 [M – (pinacolone + CO)]$^+$ (11), 101 (39), 85 (100), 57 (37).

4α-*tert*-Butyl-1α,7β,8β-trihydro-2β,4β-dimethyl-3,5-dioxa-6-oxotricyclo-[6.4.0.0^{2,7}]dodecane (9a): mp 68–70 °C; ^1H NMR ($CDCl_3$) δ 3.04 (d, *J* = 7.7 Hz, 1H, H-7), 1.90 (m, 1H, H-1), 1.60 (m, 1H, H-8), 1.50–1.15 (m, 8H, H's 9, 10, 11, and 12), 1.44 (s, 6H, 2-CH_3 and 4-CH_3), 1.04 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) (DEPT) δ 170.21 (quat, C-6), 110.36 (quat, C-4), 77.77 (quat, C-2), 55.68 (CH, C-7), 47.30 (CH, C-1), 38.89 (quat, $C(CH_3)_3$), 38.71 (CH, C-8), 28.94 (CH_2, C-9), 26.71 (CH_2, C-10), 26.35 (CH_2, C-11), 25.44 (CH_2, C-12), 24.39 (CH_3, $C(CH_3)_3$), 20.87 (CH_3, 2-CH_3), 20.02 (CH_3, 4-CH_3); IR (CCl_4) 1738, 1295, 1250, 1195, 1150, 1143, 1105, cm^{-1}; EIMS (50 eV) *m/z* (relative intensity) 267 [M + 1]$^+$ (10), 251 $[M - CH_3]^+$ (1), 209 [M – *tert*-butyl]$^+$ (6), 185 [M – cyclohexane]$^+$ (21), 167 [(M + 1) – pinacolone]$^+$ (56), 138 [M – (pinacolone + CO)]$^+$ (15), 125 (13), 101 (39), 95 (32), 85 (87), 81 (62), 57 (37), 43 (100).

Irradiation of 1 and the Ethylene Ketal of 2-Cyclohexenone. Using the general conditions, **1** (300 mg, 1.63 mmol) and the ethylene ketal of cyclohexenone (457 mg, 3.26 mmol) in 20% acetone/acetonitrile (4 mL) were irradiated for 12 h. Separation of the crude product by MPLC (20% EtOAc/hexanes) gave two crystalline products: **7b** (264 mg, 35%) and **9b** (101 mg, 14%).

4α-*tert*-Butyl-1α,7β,8α-trihydro-2β,4β-dimethyl-3,5-dioxa-9α,9β-(ethylenedioxy)-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (7b): mp 89–91 °C; ^1H NMR ($CDCl_3$) δ 3.95 (m, 4H, H's-4′ and 5′), 3.09 (d, *J* = 4.0 Hz, 1H, H-7), 2.81 (dd, *J* = 11.6, 4.0 Hz, H-8), 2.66 (dt, *J* = 11.6, 4.6 Hz, 1H, H-1), 1.79–1.35 (m, 6H, H's-10, 11, and 12), 1.51 (s, 3H, 2-CH_3), 1.47 (s, 3H, 4-CH_3), 1.03 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 172.1 (+, C-6), 110.9 (+, C-4), 107.8 (+, C-9), 77.22 (+, C-2), 65.39 (+, C-4′), 63.90 (+, C-5′), 43.89 (–, C-7), 41.76 (–, C-1), 41.28 (–, C-8), 39.30 (+, $C(CH_3)_3$), 32.10 (+, C-10), 24.48 (–, $C(CH_3)_3$), 22.18 (–, 4-CH_3), 21.10 (–, 2-CH_3), 20.01 (+, C-11), 19.77 (+, C-12); IR (CCl_4) 1734, 1297, 1249, 1216, 1125, 1098, 1076, 985 cm^{-1}; EIMS (50 eV) *m/z* (relative intensity) 267 [M – *tert*-butyl]$^+$ (3), 224 [M – pinacolone]$^+$ (21), 179 (35), 165 (22), 153 (30), 128 (64), 113 (81), 99 (100), 86 (67), 79 (46), 55 (31).

4α-*tert*-Butyl-1α,7β,8β-trihydro-2β,4β-dimethyl-3,5-dioxa-9α,9β-(ethylenedioxy)-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (9b): mp 84.0–86.0 °C; ^1H NMR ($CDCl_3$) δ 4.29 (q, *J* = 7.0 Hz, 1H, H-4′), 3.95 (m, 2H, H's 4′ and 5′), 3.78 (q, *J* = 7.0 Hz, 1H, H-5′), 3.05 (d, *J* = 8.8 Hz, 1H, H-7), 2.34 (m, 1H, H-1), 1.94 (dd, *J* = 13.9, 8.8 Hz, 1H, H-8), 1.80–1.35 (m, 6H, H's 10, 11, and 12), 1.42 (s, 3H, 2-CH_3), 1.39 (s, 3H, 4-CH_3), 1.03 (s, 9H, $C(CH_3)_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 168.77 (+, C-6), 110.15 (+, C-4), 108.53 (+, C-9), 77.65 (+, C-2), 65.55 (+, C-4′), 65.19 (+, C-5′), 52.22 (–, C-8), 45.30 (–, C-7), 43.62 (–, C-1), 38.87 (+, $C(CH_3)_3$), 37.40 (+, C-10), 25.51 (+, C-11), 24.51 (–, $C(CH_3)_3$), 24.41 (+, C-12), 21.46 (–, 4-CH_3), 20.28 (–, 2-CH_3); IR (CCl_4) 1735, 1302, 1246, 1221, 1120 cm^{-1}; EIMS (50 eV) *m/z* (relative intensity) 225 [M – pinacolone]$^+$ (37), 179 (28), 165 (26), 153(30), 128 (55), 113 (91), 99 (100), 86 (69).

Irradiation of (–)-1 (R = CD_3) and the Ethylene Ketal of 2-Cyclohexenone. Using the general conditions, (–)-1 (R = CD_3)[10] (300 mg, 1.63 mmol) and the ethylene ketal of cyclohexenone (460 mg, 3.28 mmol) in 20% acetone/acetonitrile (4 mL) were irradiated for 12 h. Separation of the crude product by MPLC (20% EtOAc/hexanes) gave two crystalline products: **10** (270 mg, 36%) and **9b** (4-CD_3) (99 mg, 14%, data not reported).

4α-*tert*-Butyl-1α,7β,8α-trihydro-2β-methyl-4β-(deuteriomethyl)-3,5-dioxa-9α,9β-(ethylenedioxy)-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (10): mp 88.0–91.0 °C; ^1H NMR ($CDCl_3$) δ 3.96 (m, 4H, H's 4′ and 5′), 3.10 (d, *J* = 4.0 Hz, 1H, H-7), 2.83 (dd, *J* = 11.6, 4.0 Hz, 1H, H-8), 2.68 (dt, *J* = 11.6, 4.6 Hz, 1H, H-1), 1.80–1.38 (m, 6H, H's 10, 11, and 12), 1.53 (s, 3H, 2-CH_3), 1.05 (s, 9H, C-$(CH_3)_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 172.1 (+, C-6), 110.7 (+, C-4), 107.6 (+, C-9), 77.09 (+, C-2), 65.26 (+, C-4′), 63.75 (+, C-5′), 43.77 (–, C-7), 41.58 (–, C-1), 41.13 (–, C-8), 39.10 (+, $C(CH_3)_3$), 31.95 (+, C-10), 24.34 (–, $C(CH_3)_3$), 20.91 (–, 2-CH_3), 19.85 (+, C-11), 19.64 (+, C-12); IR (CCl_4) 2210, 1733, 1290, 1246, 1209, 1120, 1100 cm^{-1}; EIMS (50 eV) *m/z* (relative intensity) 328 [M + 1]$^+$ (0.2), 327 $[M]^+$ (0.1), 309 $[M - CD_3]^+$ (0.2), 270 [M – *tert*-butyl]$^+$ (4), 224 [M – pinacolone-d_3] (2), 153 (6), 121 (59), 119 (100), 117 (77), 113 (28), 112 (33), 99 (30).

Major Isomer—7α-Acetyl-6β-(formylmethyl)-6α,7β-dihydro-1,4-dioxaspiro[4.5]decane (*trans*-11). Minor Isomer—7β-Acetyl-6β-(formylmethyl)-6α,7α-dihydro-1,4-dioxaspiro[4.5]decane (*cis*-11). To a solution of adduct **10** (37 mg, 0.13 mmol) in dry toluene (5 mL) under argon at –78 °C was added dropwise diisobutylaluminum hydride (120 μL of 1.5 M solution in toluene, 0.18 mmol). After stirring the solution for 1.5 h at –78 °C, dry MeOH (3 mL) was added and the temperature was allowed to warm to –10 °C. A 10% HCl solution (4 mL) was added, and the mixture was stirred at room temperature for 1 h. The aqueous phase was extracted with ether (3×), and the combined organic phases were washed with saturated $NaHCO_3$ solution and brine and dried (anhydrous $MgSO_4$). After removal of the solvent, the residue was purified by MPLC (15% EtOAc/hexanes) to give **11** (14.4 mg, 62%) as an inseparable mixture of epimers (3:1 *trans/cis* by ^1H NMR).

Major epimer: ^1H NMR ($CDCl_3$) δ 9.53 (dd, *J* = 4.8, 1.3 Hz, 1H, C*H*O), 4.1–3.7 (m, 4H, H's 2 and 3), 2.94–1.20 (m, 10H), 2.16 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) (APT) δ 210.59 (+, *C*OCH$_3$), 200.88 (–, *C*HO), 109.55 (+, C-5), 64.96 (+, C-2), 63.90 (+, C-3), 53.68 (–, C-6), 41.92 (+, C-13), 41.39 (–, C-7), 34.12 (+, C-8), 29.83 (–, C-12), 29.10 (+, C-9), 22.84 (+, C-10). Minor epimer: ^1H NMR ($CDCl_3$) δ 9.67 (t, *J* = 0.7 Hz, 1H, C*H*O), 4.1–3.7 (m, 4H, H's 2 and 3), 2.94–1.20 (m, 10H), 2.13 (s, 3H, COCH_3); ^{13}C NMR ($CDCl_3$) (APT) δ 210.59 (+, *C*OCH$_3$), 200.88 (–, *C*HO), 109.99 (+, C-5), 64.96 (+, C-2), 64.45 (+, C-3), 51.61 (–, C-6), 40.90 (+, C-13), 37.52 (–, C-7), 30.76 (+, C-8), 29.83 (–, C-12), 21.97 (+, C-10), 21.41 (+, C-9); IR on mixture (CCl_4) 2816, 2717, 1720, 1714, 1542, 1351, 1210, 1154 cm^{-1}; EIMS on mixture (50 eV) *m/z* (relative intensity) 225 $[M - 1]^+$ (1), 199 (13), 183 [M – $COCH_3$]$^+$ (19), 177 (8), 112 (100), 99 (86).

Major Epimer—1α,6β-Dihydro-5α-methyl-10α,10β-(ethylenedioxy)-4-oxabicyclo[4.4.0]-3-decanone (*trans*-12). Minor Epimer—1α,6α-Dihydro-5α-methyl-10α,10β-(ethylenedioxy)-4-oxabicyclo[4.4.0]-3-decanone (*cis*-12). To a solution of diisobutylaluminum hydride (177 μL of a 1.5 M solution, 0.27 mmol) in dry toluene (5 mL) under argon at –78 °C was added dropwise dry MeOH (3 mL). After the mixture was stirred for 0.5 h at –78 °C, a solution of **11** (37 mg, 0.17 mmol, 3:1 mixture of isomers) in dry toluene (2 mL) was added by cannula. The reaction temperature was allowed to warm gradually to 0 °C, the solvent was removed *in vacuo*, the residue was suspended in water (5 mL), and this aqueous phase was extracted with ether (3×). The combined organic extracts were washed with brine and dried ($MgSO_4$). The solvent was removed, and the residue was purified by MPLC (25% EtOAc/hexanes) to give lactone **12** (25 mg, 67%) as a mixture of epimers (3:1 *trans/cis* by NMR).

Major epimer: ^1H NMR ($CDCl_3$) δ 4.70 (dq, *J* = 8.7, 6.4 Hz, 1H, H-5), 3.94 (m, 4H, H's 4′ and 5′), 2.70–1.20 (m, 10H, H's 1, 2, and 6–9), 1.34 (d, *J* = 6.4 Hz, 3H, 5-CH_3); ^{13}C NMR ($CDCl_3$) (APT) δ 171.17 (+, C-3), 109.15 (+, C-10), 78.26 (–, C-5), 65.00 (+, C-4′), 64.43 (+, C-5′), 39.43 (–, C-1), 38.24 (–, C-6), 32.96 (+, C-2), 29.25 (+, C-9), 25.68 (+, C-7), 20.76 (–, 5-CH_3), 19.63 (+, C-8). Minor epimer: ^1H NMR ($CDCl_3$) δ 4.56 (dq, *J* = 6.7, 4.3 Hz, 1H, H-5), 3.94 (m, 4H, H's 4′ and 5′), 2.70–1.20 (m, 10H, H's 1, 2, and 6–9), 1.26 (d, *J* = 6.7 Hz, 3H, 5-CH_3); ^{13}C NMR ($CDCl_3$) (APT) δ 171.46 (+, C-3), 108.76 (+, C-10), 77.60 (–, C-5), 65.27 (+, 4′), 64.80 (+, 5′), 38.17 (–, C-1), 37.43 (–, C-6), 34.25 (+, C-2), 28.26 (+, C-9), 26.91 (+, C-7), 22.27 (+, C-8), 16.40 (–, 5-CH_3); IR on mixture (CCl_4) 1731, 1541, 1372, 1231, 1196, 1146, 1104 cm^{-1}; EIMS on mixture (50 eV) *m/z* (relative intensity) 226 $[M]^+$ (7), 166 (8), 138 (10), 99 (100), 86 (51), 85 (55); HRMS calcd for $C_{12}H_{18}O_4$ 226.1205, found 226.1207.

Irradiation of 1 and Cyclopentene. Using the general conditions, a solution of **1** (300 mg, 1.63 mmol) and cyclopentene (222 mg, 3.26 mmol) in 20% acetone/acetonitrile (4 mL) was irradiated for 5 h. Separation of the crude product by MPLC (10% EtOAc/hexanes) gave two crystalline adducts **13a** (126 mg, 31%) and **14a** (12 mg, 2.9%) as well as recovered dioxinone **1** (202 mg). Compound **14a** eluted before **13a**. The combined adduct yield based on recovered **1** is 99%.

9α-tert-Butyl-1β,2α,6α-trihydro-7β,9β-dimethyl-8,10-dioxa-11-oxotricyclo[6.4.0.0^{2,6}]undecane (13a): mp 51.5–52.5 °C; ^{1}H NMR ($CDCl_3$) δ 2.84 (m, 1H, H-2), 2.59 (td, J = 7.9, 1.1 Hz, 1H, H-6), 2.29 (dd, J = 5.6, 1.1 Hz, 1H, H-1), 1.84–1.14 (m, 6H, H's 3–5), 1.41 (s, 3H, 9-CH_3), 1.27 (s, 3H, 7-CH_3), 1.01 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 171.7 (+, C-11), 112.3 (+, C-9), 75.7 (+, C-7), 48.4 (–, C-1), 43.3 (–, C-6), 41.9 (–, C-2), 39.4 (+, C(CH$_3$)$_3$), 31.7 (+, C-5), 26.8 (+, C-3), 25.2 (+, C-4), 24.4 (–, C(CH$_3$)$_3$), 23.0 (–, 7-CH$_3$), 21.3 (–, 9-CH$_3$); IR (CCl_4) 1731, 1372, 1288 cm^{-1}; EIMS (35 eV) m/z (relative intensity) 253 [M + 1]$^+$ (17), 195 [M – tert-butyl]$^+$ (29), 185 [M + 1 – cyclopentene]$^+$ (32), 153 [M + 1 – pinacolone]$^+$ (81), 101 (77), 85 (100); HRMS calcd for $C_{15}H_{25}O_3$ [M + 1]$^+$ 253.1803, found 253.1813.

9α-tert-Butyl-1α,2β,6β,-trihydro-7α,9β-dimethyl-8,10-dioxa-11-oxotricyclo[6.4.0.0^{2,6}]undecane (14a): mp 80.0–81.0 °C; ^{1}H NMR ($CDCl_3$) δ 2.95 (m, 2H, H's 2 and 6), 2.45 (d, 4.4 Hz, 1H, H-1), 1.96–1.34 (m, 6H, H's 3–5), 1.78 (s, 3H, 9-CH_3), 1.19 (s, 3H, 7-CH_3), 0.99 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 170.4 (+, C-11), 111.0 (+, C-9), 76.9 (+, C-7), 49.0 (–, C-1), 45.4 (–, C-6), 40.7 (+, C(CH$_3$)$_3$), 40.2 (–, C-2), 32.0 (+, C-5), 27.8 (+, C-3), 25.8 (+, C-4), 24.5 (–, C(CH$_3$)$_3$), 22.7 (–, 9-CH$_3$), 22.3 (–, 7-CH$_3$); IR (CCl_4) 1733, 1373, 1314, 1284 cm^{-1}; EIMS (35 eV) m/z (relative intensity) 253 [M + 1]$^+$ (0.5), 185 [M + 1 – cyclopentene]$^+$ (34), 101 (27), 85 (100).

Irradiation of 2 and Cyclohexene. Using the general conditions, dioxinone **2** (300 mg, 1.76 mmol) and cyclohexene (289 mg, 3.53 mmol, 2 equiv) in 20% acetone/acetonitrile (4 mL) were irradiated for 10 h. The crude mixture was separated by MPLC (10% EtOAc/hexanes) to give seven adducts **16–22** (combined mass 414 mg, 93%). Integration of the acetal protons H-4 in the ^{1}H NMR spectrum of the adduct mixture gave the following product distribution: **16** (32%), **17** (14%), **18** (4%), **19** (15%), **20** (15%), **21** (13%), and **22** (7%). In the MPLC separation, components **16–18** eluted before **19–22**. The structures were tentatively assigned on the basis of the following ^{1}H NMR spectra, and in some cases it was necessary to analyze "enriched" samples because of the complexity of the product mixture.

4α-tert-Butyl-1α,4β,7α,8α-tetrahydro-2α-methyl-3,5-dioxa-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (16): ^{1}H NMR ($CDCl_3$) δ 5.58 (s, 1H, H-4), 2.99 (d, J = 9.6 Hz, 1H, H-7), 2.20 (m, 1H), 1.95–1.75 (m, 5H), 1.55–1.30 (m, 4H), 1.35 (s, 3H, 2-CH_3), 0.99 (s, 9H, C(CH_3)$_3$).

4α-tert-Butyl-1β,4β,7α,8β-tetrahydro-2α-methyl-3,5-dioxa-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (17): ^{1}H NMR ($CDCl_3$) δ 5.36 (s, 1H, H-4), 2.79 (dd, J = 5.9, 1.5 Hz, 1H, H-7), 2.63 (m, 1H, H-1), 2.49 (m, 1H, H-8), 1.70–1.25 (m, 8H, H's 9–12), 1.36 (s, 3H, 2-CH_3), 1.00 (s, 9H, C(CH_3)$_3$).

4α-tert-Butyl-1β,4β,7α,8α-tetrahydro-2α-methyl-3,5-dioxa-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (18): ^{1}H NMR ($CDCl_3$) δ 5.23 (s, 1H, H-4), 2.87 (d, J = 8.7 Hz, 1H, H-7), 2.63 (m, 1H, H-1), 1.70–1.25 (m, 9H, H's 8 and 9–12), 1.36 (s, 3H, 2-CH_3), 0.98 (s, 9H, C(CH_3)$_3$).

4α-tert-Butyl-1β,4β,7β,8α-tetrahydro-2β-methyl-3,5-dioxa-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (19): ^{1}H NMR ($CDCl_3$) δ 4.98 (s, 1H, H-4), 2.57 (d, J = 9.1 Hz, 1H, H-7), 2.07 (m, 1H, H-8), 1.92 (br d, J = 10.0 Hz, 1H, H-1), 1.85–1.25 (m, 8H), 1.37 (s, 3H, 2-CH_3), 1.01 (s, 9H, C(CH_3)$_3$).

4α-tert-Butyl-1α,4β,7β,8α-tetrahydro-2β-methyl-3,5-dioxa-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (20): ^{1}H NMR ($CDCl_3$) δ 4.94 (s, 1H, H-4), 2.75 (ddd, J = 8.4, 6.4, 6.3 Hz, 1H, H-8), 2.65 (d, J = 6.4 Hz, 1H, H-7), 2.35 (dd, J = 16.8, 8.4 Hz, 1H, H-1), 1.85–1.65 (m, 2H), 1.65–1.50 (m, 2H), 1.50–1.40 (m, 2H), 1.37 (s, 3H, 2-CH_3), 1.32–1.20 (m, 2H), 0.99 (s, 9H, C(CH_3)$_3$).

4α-tert-Butyl-1α,4β,7β,8β-tetrahydro-2β-methyl-3,5-dioxa-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (21): ^{1}H NMR ($CDCl_3$) δ 4.77 (s, 1H, H-4), 2.92 (d, J = 8.0 Hz, 1H, H-7), 1.93 (m, 1H, H-8), 1.85–1.70 (m, 3H), 1.70–1.58 (m, 3H), 1.39 (s, 3H, 2-CH_3), 1.35–1.20 (m, 3H), 0.97 (s, 9H, C(CH_3)$_3$).

4α-tert-Butyl-1β,4β,7β,8β-tetrahydro-2β-methyl-3,5-dioxa-6-oxotricyclo[6.4.0.0^{2,7}]dodecane (22): ^{1}H NMR ($CDCl_3$) δ 4.90 (s, 1H, H-4), 2.92 (d, J = 9.5 Hz, 1H, H-7), 2.70 (m, 1H, H-8), 2.32 (m, 1H, H-1), 1.80–1.30 (m, 8H), 1.38 (s, 3H, 2-CH_3), 1.01 (s, 9H, C(CH_3)$_3$).

Irradiation of 2 and Cyclopentene. Using the general conditions, dioxinone **2** (300 mg, 1.76 mmol) and cyclopentene (240 mg, 3.53 mmol) in 20% acetone/acetonitrile (4 mL) were irradiated for 10 h. The crude product was separated by MPLC (15% EtOAc/hexanes) to give **13b** (56 mg, 13%), **14b** (123 mg, 29%), **15** (46 mg, 11%), and recovered **2** (120 mg). The combined yield based on recovered **2** was 89%. Adduct **14b** eluted first and was a clear oil while **13b** and **15** were inseparable and the mixture appeared as a white solid.

9α-tert-Butyl-1β,2α,6α,9β-tetrahydro-7β-methyl-8,10-dioxa-11-oxotricyclo[6.4.0.0^{2,6}]undecane (13b): ^{1}H NMR ($CDCl_3$) δ 4.87 (s, 1H, H-9), 2.95 (m, 1H, H-2), 2.62 (td, J = 7.7, 1.3 Hz, 1H, H-6), 2.24 (dd, J = 5.6, 1.3 Hz, 1H, H-1), 1.90–1.30 (m, 6H, H's 3–5), 1.18 (s, 3H, 7-CH_3), 0.97 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 172.3 (+, C-11), 103.1 (–, C-9), 77.2 (+, C-7), 46.6 (–, C-1), 44.7 (–, C-6), 41.7 (–, C-2), 34.6 (+, C(CH$_3$)$_3$), 31.7 (+, C-5), 26.7 (+, C-3), 26.0 (+, C-4), 23.9 (–, C(CH$_3$)$_3$), 17.1 (–, 7-CH$_3$); IR (CCl_4) (mixture with **15**) 1741, 1252, 1236, 1221 cm^{-1}; EIMS on mixture (35 eV) m/z (relative intensity) 239 [M + 1]$^+$ (12), 171 [M + 1 – cyclopentene]$^+$ (55), 153 [M + 1 – pivaldehyde]$^+$ (81), 124 (89), 85 (100); HRMS calcd for $C_{14}H_{23}O_3$ [M + 1]$^+$ 239.1647, found 239.1656.

9α-tert-Butyl-1α,2β,6β,9β-tetrahydro-7α-methyl-8,10-dioxa-11-oxotricyclo[6.4.0.0^{2,6}]undecane (14b): ^{1}H NMR ($CDCl_3$) δ 5.42 (s, 1H, H-9), 2.82 (m, 1H, H-2), 2.74 (dd, J = 7.8, 7.8 Hz, 1H, H-6), 2.44 (d, J = 5.6 Hz, 1H, H-1), 1.92–1.35 (m, 6H, H's 3–5), 1.14 (s, 3H, 7-CH_3), 0.96 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 170.8 (+, C-11), 101.5 (–, C-9), 76.5 (+, C-7), 47.8 (–, C-1), 46.5 (–, C-6), 38.3 (–, C-2), 34.7 (+, C(CH$_3$)$_3$), 31.9 (+, C-5), 27.5 (+, C-3), 25.1 (+, C-4), 24.0 (–, C(CH$_3$)$_3$), 20.5 (–, 7-CH$_3$); IR (CCl_4) 1740, 1278, 1242 cm^{-1}; EIMS (35 eV) m/z (relative intensity) 239 [M + 1]$^+$ (25), 171 [M + 1 – cyclopentene]$^+$ (72), 153 [M + 1 – pivaldehyde]$^+$ (79), 124 (61), 85 (100); HRMS calcd for $C_{14}H_{23}O_3$ [M + 1]$^+$ 239.1647, found 239.1637.

9α-tert-Butyl-1β,2β,6β,9β-tetrahydro-7β-methyl-8,10-dioxa-11-oxotricyclo[6.4.0.0^{2,6}]undecane (15): ^{1}H NMR ($CDCl_3$) δ 4.75 (s, 1H, H-9), 2.95 (m, 1H, H-2), 2.86 (dd, J = 10.6, 1.5 Hz, 1H, H-1), 2.62 (td, J = 7.7, 1.3 Hz, 1H, H-6), 1.90–1.30 (m, 6H, H's 3–5), 1.39 (s, 3H, 7-CH_3), 0.95 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 170.4 (+, C-11), 102.4 (–, C-9), 73.5 (+, C-7), 47.6 (–, C-1), 42.1 (–, C-6), 36.5 (–, C-2), 34.7 (+, C(CH$_3$)$_3$), 28.4 (+, C-5), 26.0 (+, C-4), 25.2 (+, C-3), 24.9 (–, 7-CH$_3$), 23.9 (–, C(CH$_3$)$_3$); IR see **13b**; EIMS see **13b**.

Methyl 5-Hydroxy-5,6,6-trimethyl-3-oxoheptanoate (24). A solution of 1-methoxy-1,3-bis(trimethylsiloxy)-1,3-butadiene (**23**)[22] (6.12 g, 23.4 mmol) and pinacolone (2.34 g, 23.4 mmol) in dry CH_2Cl_2 (30 mL) was cooled to –78 °C under argon. $TiCl_4$ (2.57 mL, 23.4 mmol) was added, and the solution was maintained at –78 °C for 4 h, after which it was quickly poured into a saturated solution of $NaHCO_3$ (20 mL). The mixture was stirred at room temperature for 30 min, and then the aqueous phase was extracted with ether (3×). The combined organic phases were washed with H_2O and with brine and dried ($MgSO_4$). After removal of the solvent, the residue was purified by MPLC (20% EtOAc/hexanes) to yield **24** (3.63 g, 72%) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 3.67 (s, 3H, OCH_3), 3.48 (s, 2H, H-2), 3.11 (br s, 1H, -OH), 2.77, 2.57 (AM q, J = 15.8 Hz, 2H, H-4), 1.15 (s, 3H, C5-CH_3), 0.87 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 205.5 (+, C-3), 167.4 (+, C-4), 75.6 (+, C-5), 52.2 (–, OCH$_3$), 50.7 (+, C-2), 47.6 (+, C-4), 37.8 (+, C-6), 24.84 (–, C(CH$_3$)$_3$), 21.8 (–, 5-CH$_3$); IR (CCl_4) 1750, 1716, 1320, 1245, 1158 cm^{-1}; CIMS (NH_3) m/z (relative intensity) 234 [(M + 1) + NH_3]$^+$ (28), 217 [M + 1]$^+$ (6), 199 [(M + 1) – H_2O]$^+$ (100).

6-tert-Butyl-5,6-dihydro-4-hydroxy-6-methyl-2H-pyran-2-one (25). A mixture of **24** (3.63 g, 16.8 mmol) in 0.1 M NaOH solution (750 mL) was stirred at room temperature for 2 h. Following extraction with ether, the aqueous phase was cooled to 0 °C and acidified to pH 1 with 2 M HCl. Ether (175 mL) was added, the mixture was stirred for 15 min, the layers were separated, and the aqueous phase was extracted with ether (3×) while maintaining the pH at 1. The combined ether extracts were washed with brine and dried ($MgSO_4$). Removal of the solvent and recrystallization of the solid product from $CHCl_3$/pentane gave **25** (2.21 g, 71%) as small off-white crystals: mp 116–117 °C; ^{1}H NMR ($CDCl_3$) δ 3.40 (s, 2H, H-3), 2.82, 2.59 (AM q, J = 15.9 Hz, H-5), 1.34 (s, 3H, C6-CH_3), 1.05 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 201.6 (+, C-4), 167.7 (+, C-2), 85.7 (+, C-6), 44.9 (+, C-3), 44.0 (+, C-5), 37.8 (+, C(CH$_3$)$_3$), 24.8 (–, C-(CH$_3$)$_3$), 21.7 (–, 6-CH$_3$); IR ($CHCl_3$) 1725 (br), 1420, 1365, 1214 cm^{-1}; EIMS (70 eV) m/z (relative intensity) 185 [M + 1]$^+$ (3), 127 [M – C(CH$_3$)$_3$]$^+$ (40), 100 (14), 85 (33), 57 (43), 43 (100); HRMS calcd for $C_{10}H_{17}O_3$ [M + 1]$^+$ 185.1177, found 185.1194. Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.77; H, 7.65.

6-tert-Butyl-5,6-dihydro-4-methoxy-6-methyl-2H-pyran-2-one (26). To a solution of **25** (250 mg, 1.36 mmol) and trimethyl orthoformate (193 μL, 187 mg, 1.77 mmol) in dry $CHCl_3$ (2 mL) under argon was added with stirring two drops of concentrated H_2SO_4. After the mixture was stirred for 20 h at room temperature, the solvent and excess reagent were removed *in vacuo*. The crude product was purified directly by MPLC (20% EtOAc/hexanes) to give crystalline **26** (265 mg, 98%): mp 87–88 °C; ^{1}H NMR ($CDCl_3$) δ 5.15 (d, J = 1.8 Hz, 1H, H-3), 3.73 (s,

3H, OCH_3), 2.83 (dd, J = 17.2, 1.8 Hz, 1H, H-5β), 2.05 (d, J = 17.2 Hz, 1H, H-5α), 1.37 (s, 3H, 6-CH_3), 1.01 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 171.8 (+, C-2), 166.3 (+, C-4), 89.2 (–, C-3), 84.0 (+, C-6), 55.6 (–, OCH_3), 37.2 (+, C(CH$_3$)$_3$), 32.8 (+, C-5), 24.5 (–, C(CH_3)$_3$), 19.4 (–, 6-CH_3); IR (CCl_4) 1709, 1634, 1369, 1226, 1206 cm^{-1}; EIMS (70 eV) m/z (relative intensity) 183 [M – CH_3]$^+$ (5), 169 (39), 149 (27), 141 (28), 125 (34), 111 (62), 85 (100); CIMS (NH_3) m/z (relative intensity) 199 [M + 1]$^+$ (100). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.67; H, 9.09. Found: C, 66.56; H, 9.65.

6-*tert*-Butyl-5,6-dihydro-4,6-dimethyl-2*H*-pyran-2-one (4). A stirred suspension of CuI (516 mg, 2.72 mmol) in dry ether (4 mL) was cooled to 0 °C, and methyllithium (3.88 mL of a 1.4 M solution in hexanes, 5.43 mmol) was added dropwise over 20 min. After the mixture was cooled to –78 °C, a solution of **26** (140 mg, 0.707 mmol) and trimethylsilyl chloride (138 μL, 118 mg, 1.09 mmol) in dry ether (2 mL) was added dropwise by cannula. The reaction mixture was allowed to warm to –20 °C over 2 h, a 1:1 NH_3/saturated NH_4Cl solution (12 mL) was added, and the mixture was stirred until a dark-blue color persisted. The aqueous phase was extracted with ether (3×), and the combined ether layers were washed with brine and dried ($MgSO_4$). Removal of the solvent and purification of the residue by MPLC (20% EtOAc/hexanes) provided the crystalline solid **4** (95 mg, 74%): mp 80–81 °C; ^{1}H NMR ($CDCl_3$) δ 5.73 (br s, 1H, H-3), 2.62 (br d, J = 18.0 Hz, 1H, H-5β), 1.91 (d, J = 18.0 Hz, 1H, H-5α), 1.90 (br s, 3H, 4-CH_3), 1.27 (s, 3H, 6-CH_3), 0.95 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 164.5 (+, C-2), 155.6 (+, C-4), 115.5 (–, C-3), 85.6 (+, C-6), 37.5 (+, C(CH$_3$)$_3$), 34.9 (+, C-5), 24.8 (–, C(CH_3)$_3$), 23.3 (–, 4-CH_3), 19.9 (–, 6-CH_3); IR (CCl_4) 1714 (br), 1382, 1150 cm^{-1}; EIMS (70 eV) m/z (relative intensity) 125 [M – C(CH_3)$_3$)]$^+$ (100); CIMS (NH_3) m/z (relative intensity) 183 [M + 1]$^+$ (100); HRMS calcd for $C_{11}H_{19}O_2$ [M + 1]$^+$ 183.1385, found 183.1387.

4β-*n*-Butyl-6α-*tert*-butyl-tetrahydro-4α,6β-dimethyl-2*H*-pyran-2-one (27). Using the general cuprate procedure, CuI (672 mg, 3.54 mmol), *n*-butyllithium solution (4.42 mL, 7.07 mmol) and lactone **4** (214 mg, 1.18 mmol) were reacted and the crude product was purified by MPLC (5% EtOAc/hexanes) to give **27** (184 mg, 65%) as a clear oil: ^{1}H NMR ($CDCl_3$) δ 2.38 (dd, J = 16.3, 1.3 Hz, 1H, H-3β), 2.10 (d, J = 16.3 Hz, 1H, H-3α), 1.76 (d, J = 14.0 Hz, 1H, H-5α), 1.49 (br d, J = 14.0 Hz, 1H, H-5β), 1.35 (s, 3H, 6-CH_3), 1.34–1.16 (m, 6H), 0.96 (s, 3H, 4-CH_3), 0.95 (s, 9H, C-(CH_3)$_3$), 0.89 (t, J = 6.5 Hz, 3H, 4′-CH_3); ^{13}C NMR ($CDCl_3$) (APT) δ 172.5 (+, C-2), 87.2 (+, C-6), 42.1 (+, C-3), 40.9 (+, C-4), 39.3 (+, C(CH$_3$)$_3$), 38.8 (+, C-5), 33.2 (+, C-1′), 27.9 (–, 6-CH_3), 26.0 (+, C-2′), 24.7 (–, 4-CH_3), 24.7 (–, C(CH_3)$_3$), 23.2 (C-3′), 14.0 (–, C-4′); IR (CCl_4) 1737, 1302, 1276 cm^{-1}; EIMS (70 eV) m/z (relative intensity) 241 [M + 1]$^+$ (3), 225 [M – CH_3)]$^+$ (6), 183 [M – C(CH_3)$_3$)]$^+$ (87), 155 (17), 125 (100), 83 (31), 57 (47); CIMS (NH_3) m/z (relative intensity) 258 [(M + 1) + NH_3]$^+$ (59), 241 [M + 1]$^+$ (100); HRMS calcd for $C_{15}H_{29}O_2$ [M + 1]$^+$ 241.2167, found 241.2163.

2-*tert*-Butyl-2,3-dihydro-2,6-dimethyl-4*H*-pyran-4-one (5). To a solution of 2,4-bis(trimethylsiloxy)-1,3-pentadiene (**28**) (5.85 g, 23.9 mmol) and pinacolone (2.98 mL, 23.9 mmol) in dry CH_2Cl_2 (10 mL) at –78 °C under argon was added with stirring $TiCl_4$ (3.58 mL, 32.7 mmol), and the reaction was maintained at this temperature for 4 h. The solution was poured rapidly into saturated $NaHCO_3$ solution (20 mL), and the biphasic mixture was stirred at room temperature for 30 min. The aqueous phase was separated and extracted with ether (3×), and the combined layers were washed with water and brine and dried ($MgSO_4$). The solvent was removed, and the residue was purified by MPLC (25% EtOAc/hexanes) to yield **5** (1.04 g, 24%) as a colored oil: ^{1}H NMR ($CDCl_3$) δ 5.13 (br s, 1H, H-5), 2.59 (br d, J = 16.2 Hz, 1H, H-3β), 2.02 (d, J = 16.2 Hz, 1H, H-3α), 1.82 (s, 3H, 6-CH_3), 1.16 (br s, 3H, 2-CH_3), 0.87 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 199.6 (+, C-4), 172.0 (+, C-6), 102.5 (–, C-5), 86.9 (+, C-2), 40.8 (+, C-3), 37.2 (+, C(CH$_3$)$_3$), 24.7 (–, C(CH_3)$_3$), 21.2 (–, 6-CH_3), 16.7 (2-CH_3); IR (CCl_4) 1673, 1620, 1400, 1360 cm^{-1}; EIMS (70 eV) m/z (relative intensity) 183 [M + 1]$^+$ (100), 167 [M – CH_3]$^+$ (50), 125 [M – C(CH_3)$_3$]$^+$ (95), 85 [$C_4H_5O_2$]$^+$ (43), 83 (45); HRMS calcd for $C_{11}H_{19}O_2$ [M + 1]$^+$ 183.1385, found 183.1392.

2-*tert*-Butyl-2,3-dihydro-6-methyl-4*H*-pyran-4-one (29). Following the same procedure as described above for the preparation of **5**, the bis-trimethylsiloxy diene **28** (5.85 g, 23.9 mmol) and pivaldehyde (2.59 mL, 23.9 mmol) in dry CH_2Cl_2 (10 mL) were reacted with $TiCl_4$ (3.58 mL, 32.7 mmol) and purified by MPLC (25% EtOAc/hexanes) to yield pale-yellow crystals of **29** (3.77 g, 94%): mp 34.0–34.5 °C; ^{1}H NMR ($CDCl_3$) δ 5.19 (s, 1H, H-5), 3.88 (dd, J = 13.6, 4.4 Hz, 1H, H-2), 2.54-2.14 (AB-mult, 2H, H's 3α and β), 1.90 (s, 3H, 6-CH_3), 0.89 (s, 9H, C(CH_3)$_3$); ^{13}C NMR ($CDCl_3$) (APT) δ 193.5 (+, C-4), 174.6 (+, C-6), 104.3 (–, C-5), 86.4 (–, C-2), 36.0 (+, C-3), 33.5 (+, C(CH$_3$)$_3$), 25.2 (–, C(CH_3)$_3$), 20.7 (–, 6-CH_3); IR (CCl_4) 1673, 1619, 1398, 1334, 1028 cm^{-1}; EIMS (50 eV) m/z (relative intensity) 168 [M]$^+$ (27), 153 [M – CH_3]$^+$ (14), 140 (9), 125 (8), 111 [M – (C(CH$_3$)$_3$)]$^+$ (31), 85 (100), 69 (69); HRMS calcd for $C_{11}H_{18}O_2$ 168.1150, found 168.1151.

6-*n*-Butyl-2-*tert*-butyl-tetrahydro-2,6-dimethyl-4*H*-pyran-4-one (30a/30b). Following the general cuprate procedure, CuI (626 mg, 3.29 mmol), *n*-butyllithium solution (4.12 mL, 6.59 mmol), and **5** (200 mg, 1.10 mmol) were reacted and the product was purified by MPLC (5% EtOAc/hexanes) to give **30a/30b** (167 mg, 63%) as a 50:50 mixture (by ^{1}H NMR) of inseparable isomers: ^{1}H NMR ($CDCl_3$) δ 2.64–1.98 (m, 8H), 1.56-1.20 (m, 12H), 1.17 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 1.13 (s, 3H), 0.88 (s, 18H), 0.85 (t, J = 7.3 Hz, 6H); ^{13}C NMR ($CDCl_3$) (APT) δ 210.4 (+), 210.1 (+), 81.0 (+), 79.5 (+), 76.7 (+), 75.4 (+), 50.4 (+), 49.2 (+), 46.2 (+), 45.3 (+), 45.0 (+), 43.0 (+), 39.2 (+), 38.5 (+), 29.2 (–), 27.5 (–), 26.0 (+), 25.8 (+), 24.9 (–) (coincident peaks for both isomers), 23.7 (–), 23.4 (–), 23.0 (+) (coincident peaks for both isomers), 14.0 (–) (coincident peaks for both isomers); IR (CCl_4) 1716, 1379, 1298 cm^{-1}; EIMS (50 eV) m/z (relative intensity) 241 [M + 1]$^+$ (26), 225 [M – CH_3]$^+$ (32), 184 (50), 183 [M – (C_4H_9)]$^+$ (75), 141 (71), 126 (61), 125 (100); CIMS (NH_3) m/z (relative intensity) 258 [(M + 1) + NH_3]$^+$ (34), 241 [M + 1]$^+$ (60), 223 (17), 183 (38), 141 (100), 125 (52).

2β-*n*-Butyl-6α-*tert*-butyl-tetrahydro-2α-methyl-4*H*-pyran-4-one (31). Following the general cuprate procedure, CuI (679 mg, 3.57 mmol), *n*-butyllithium solution (4.46 mL, 7.14 mmol), and **29** (200 mg, 1.20 mmol) were reacted and the product was purified by MPLC (5% EtOAc/hexanes) to yield only one product, **31** (211 mg, 78%), as a pale-yellow oil: ^{1}H NMR ($CDCl_3$) δ 3.34 (dd, J = 10.2, 4.0 Hz, 1H, H-6), 2.33-2.06 (m, 4H, H's 3 and 5), 1.56–1.40 (m, 1H), 1.30–1.14 (m, 5H), 1.20 (s, 3H, 2-CH_3), 0.87 (s, 9H, C(CH_3)$_3$), 0.84 (t, 3H, 4′-CH_3); ^{13}C NMR ($CDCl_3$) (APT) δ 209.8 (+, C-4), 77.1 (–, C-6), 76.1 (+, C-2), 53.0 (+, C-3), 42.2 (+, C-5), 35.2 (+, C(CH$_3$)$_3$), 34.3 (+, C-1′), 27.3 (–, 2-CH_3), 25.5 (–, C(CH_3)$_3$), 24.3 (+, C-2′), 23.2 (+, C-3′), 14.0 (–, C-4′); IR (CCl_4) 1716, 1379, 1298 cm^{-1}; CIMS (NH_3) m/z (relative intensity) 244 [(M + 1) + NH_3]$^+$ (100), 227 [M + 1]$^+$ (18), 169 [M – C(CH_3)$_3$]$^+$ (43), 127 (15), 111 (17); HRMS calcd for $C_{14}H_{27}O_2$ [M + 1]$^+$ 227.2011, found 227.2013.

Theoretical Predictions. Theoretical studies were carried out with the GAUSSIAN 90 and GAUSSIAN 92 program packages[41] on Silicon Graphics 4D-340 or 4D-380 workstations. Closed-shell Hartree–Fock methods[42] with a 6-31G* basis set[43] were used. Minima were located using analytic energy gradient methods and the algorithms of Schlegel.[44] No symmetry constraints were placed on the molecules. All stationary points located were characterized by determining the harmonic vibrational frequencies using analytic second-derivative[45] methods at the SCF level and found to be minima. Structures also were optimized at a level including electron correlation, namely Møller–Plesset perturbation theory at second order (MP2).[46] Analytic MP2 gradients[45,47] using the frozen core approximation were employed in these geometry optimizations. The geometries of a few substituted molecules were optimized at the MNDO[48] semiempirical level to provide an initial assessment of the effects of

(41) (a) Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M.; Binkley, J. S.; Gonzalez, C.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J.J.P.; Topiol, S.; Pople, J. A. *Gaussian 90*, Revision F; Gaussian, Inc.: Pittsburgh, PA, 1990. (b) Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P.M.W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M.A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *Gaussian 92*, Revision B; Gaussian, Inc.: Pittsburgh, PA, 1992.

(42) (a) Hartree, D. R. *Proc. Cambridge Philos. Soc.* **1928**, *24*, 89, 111, 246. (b) Fock, V. *Z. Phys.* **1930**, *61*, 126. (c) Roothaan, C. C. J. *Rev. Mod. Phys.* **1951**, *23*, 69.

(43) (a) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257. (b) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654. (c) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

(44) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214.

(45) Pople, J. A.; Krishnan, R.; Schlegel, H. B.; Binkley, J. S. *Int. J. Quantum Chem., Symp.* **1979**, *13*, 225.

(46) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

(47) (a) Frisch, M. J.; Head-Gordon, M.; Pople, J. A. *Chem. Phys. Lett.* **1990**, *166*, 275. (b) Frisch, M. J.; Head-Gordon, M.; Pople, J. A. *Chem. Phys. Lett.* **1990**, *166*, 281.

(48) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

substituents on the structures. The PSI88 package[49] was used to plot the molecular orbitals.

X-ray Crystal Structure Determinations. The data were collected at the University of Waterloo on a Siemens R3m/V diffractometer employing Mo Kα radiation (λ = 0.71073 Å) and a graphite monochromator. The structures were solved by direct methods and refined by full-matrix least-squares methods using Siemens SHELXLT PLUS software. Full details of the X-ray analyses are included in the supplementary material.

Dioxinone 1. Crystals of $C_{10}H_{16}O_3$, M = 184.2, are monoclinic, space group $P2_1/c$, a = 16.523(4), b = 5.785(1), and c = 11.517(3) Å, β = 109.39(2)°, V = 1038.4(4) Å^3, with Z = 4, D_c = 1.178 g/cm^3, F(000) = 400, and T = 200 K. Crystal dimensions were 0.26{100} × 0.60{010} × 0.54{001} mm^3. From 1833 independent reflections measured by the ω scan method ($2\theta \leq 50°$), 1408 (with $F > 6.0\sigma(F)$) were considered observed and used in the structure solution and refinement to give R and R_w values of 6.83 and 6.99%.

Adduct 7a. Crystals of $C_{16}H_{26}O_3$, M = 266.4, are monoclinic, space group $P2_1/n$, a = 14.950(8), b = 6.693(4), and c = 16.231(9) Å, β = 110.15(5)°, V = 1524.7(15) Å^3, with Z = 4, D_c = 1.160 g/cm^3, F(000) = 584, and T = 295 K. Crystal dimensions were 2.60{010} × 0.36{101} × 0.15{10$\bar{1}$} mm^3. Due to very facile cleavage parallel to 10$\bar{1}$, the needle length could not be reduced without damage to the crystal. From 2702 independent reflections measured by the ω scan method ($2\theta \leq 50°$), 1897 (with $F > 6.0\sigma(F)$) were considered observed and used in the structure solution and refinement to give R and R_w values of 5.00 and 6.10%.

(49) Jorgensen, W. L.; Severance, D. L. Unpublished extended version of PSI/77. Jorgensen, W. L. *QCPE* **1980**, *12*, program 340.

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Supplementary Material Available: Tables of crystal data, data collection conditions, solution and refinement details, atomic coordinates and equivalent isotropic displacement coefficients, bond lengths, bond angles, anisotropic displacement coefficients, H-atom coordinates and isotropic displacement coefficients for **1** and **7a**, SCF- and MP2-optimized geometries in Z-matrix or cartesian coordinate (standard orientation) form, and the SCF atomic charges for the four unsubstituted systems (20 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.