Enantioselective Synthesis of Spiro Ethers and Spiro Ketals *via* Photoaddition of Dihydro-4-pyrones to Chiral 1,3-Dioxin-4-ones†

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A versatile and highly stereoselective synthesis of spiro ethers and spiro ketals is presented. The key step in the developed synthetic sequence is based on diastereoselective intramolecular photoaddition of dihydro-4-pyrones to chiral 1,3-dioxin-4-ones. Subsequent fragmentation of the produced four-membered ring provides spiro ether structures. The spiro ethers can be transformed to their corresponding spiro ketals, with retention of configuration at the spiro center, *via* Baeyer−Villager oxidation. The configuration of the spiro center is defined by the facial selectivity at the photocycloaddition step. Two examples of complete stereofacial selectivity were achieved. The unique and important application of the developed sequence was demonstrated in enantioselective synthesis of a less thermodynamically stable spiro ketal **43**.

Introduction

The spiro ketal unit can be found as a substructure in a wide variety of naturally occurring compounds isolated from many sources, including plants, insects, microbes, fungi, and marine organisms;[1] for example, it is found in the milbemycin/avermectin macrolides,[2] which possess significant antibiotic as well as insecticidal activity,[3] antitumor toxic metabolites from blue-green algae,[4] and the talaromycins,[5,6] which represent a class of spiro ketal mycotoxins. The increasing pharmacological importance of such compounds and their synthetically challenging structures have led to intense interest in the synthesis and chemical reactivity of these compounds. The conventional synthetic approaches to spiro ketals involve acid-promoted intramolecular spiro cyclization of acyclic dihydroxy ketones or their equivalents.[1] The stereochemistry of the spiro center results from a balance between anomeric stabilization and the preference of substituents for equatorial orientation. Mixtures of products are obtained and tedious separations required when these factors are in conflict.[6] Thermodynamically less stable spiro ketal structure in talaromycins C and D were proposed in the biosynthetic pathway as the precursors of other biologically active thermodynamically more stable isomers talaromycins A, B, E, and F (Figure 1). Talaromycins A and B have been synthesized[6] by utilizing the thermodynamic stability of the spiro ketal systems. To the best of our knowledge, the synthesis of the thermodynamically less stable metabolites, talaromycins D and F, has not yet been reported.

Stereoselective synthesis of spiro ethers is still a challenge, as could be seen, for example, in the recently reported synthesis of oscilatoxin D.[7] A mixture of isomeric spiro ethers was obtained upon treatment of **7** with camphorsulfonic acid (CSA), the desired spiro ether **8** being obtained in 12% yield (Scheme 1).

We have recently been interested in developing a versatile and highly stereoselective method for the synthesis of spiro structures that allows enantioselective synthesis of spiro ethers and thermodynamically less stable spiro ketals.[8] The synthetic sequence is summarized in the following retrosynthetic scheme (Scheme 2). The key step is based on a diastereoselective intramolecular photocycloaddition of chiral 1,3-dioxin-4-one[9] to dihydro-4-pyrone[10] in photosubstrates of type **12**. Stereofacial selective photocyclization introduces four stereogenic centers with the corresponding configurations defined by the approach of the chiral dioxinone ($R_1 \neq R_2$) toward the dihydropyrone. The dioxinone functionality[11] plays four important roles: (a) it provides the desired C=C double bond, incorporated in the photocycloaddition reaction; (b) it enables selective fragmentation of the produced four-membered ring; (c) it introduces a ketone

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(11) For elegant synthetic applications of the intramolecular photoadditions of dioxinones to alkenes, see: Winkler, J. D.; Bowen, C. M.; Liotta, F. *Chem. Rev.* **1995**, *95*, 2003.

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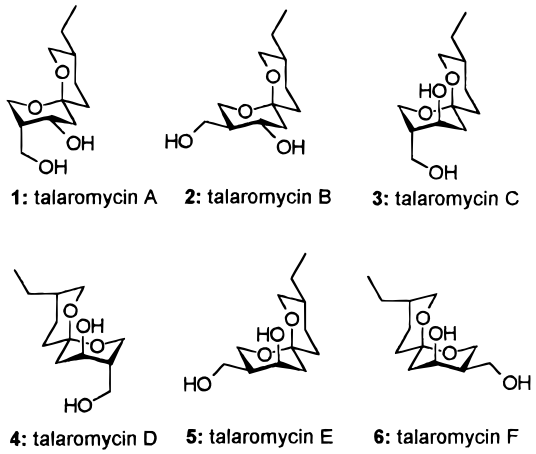
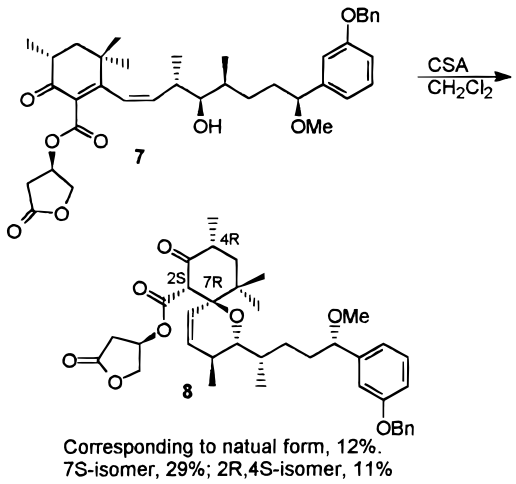
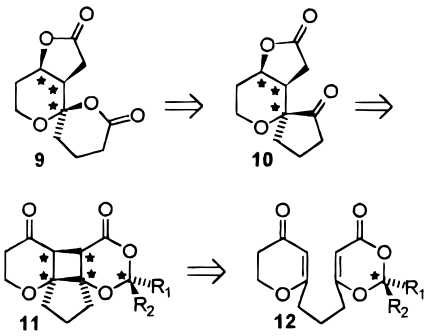


Figure 1. Talaromycins A-F (Reference 5).

Scheme 1



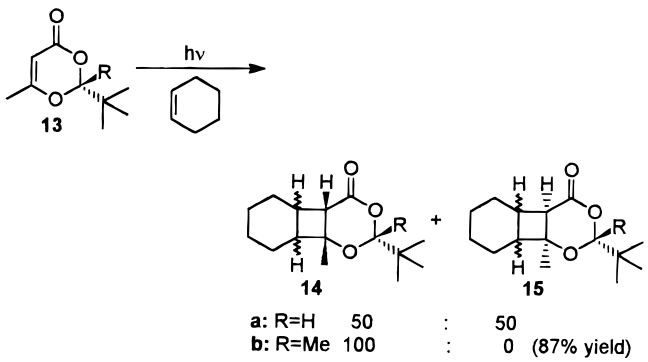
Scheme 2



functionality at the spiro ring, necessary for oxidative enlargement leading to spiro ketals; and (d) it provides for asymmetric induction.

High stereofacial selectivity in the *intermolecular* photocycloaddition of alkenes to chiral dioxinones was first reported by the pioneering studies of Demuth and co-workers[12] on the photocycloaddition of a chiral 1,3-dioxin-4-one, possessing a (−)-menthone auxiliary, to cyclic alkenes. Poor facial selectivity was obtained in the *intermolecular* photoaddition of dioxinone **13a** to various alkenes (Scheme 3). However, Lange and co-workers[13] have succeeded in obtaining high facial selectivity in the

Scheme 3



photocycloaddition of dioxinone **13b** with the preferred approach of the alkene being from the equatorial *tert*-butyl side. The observed stereoselectivity was attributed to the steric hindrance of the axial methyl at the ketal center.

Stereoselective *intramolecular* photocycloaddition of alkenes to enones with a chiral auxiliary located at the enone chromophore, which can be expected to be of general application, is not a well-explored approach. The first example of a very high stereofacial selectivity in the *intramolecular* photocycloaddition of alkenes to chiral dioxinones was recently reported by Sato and Kaneko.[14]

Results and Discussion

Preparation of the Photosubstrates. The synthesis of photosubstrates **29**−**32** is general and based on coupling of the corresponding bromide of dihydropyrone **16** (Scheme 4) with diethyl malonate,[15] followed by another coupling reaction with the corresponding dioxinones **22**, **25**, **26**, and **28** (Scheme 5). Dihydropyrone **16** was prepared by dianion condensation of acetylacetone with formaldehyde,[16] followed by cyclization of the corresponding β-diketo β'-alcohol[17] under acidic conditions (3 N HCl). Allylic radical bromination[18] of **16** with 1 equiv of *N*-bromosuccinimide (NBS) and 0.1 equiv of 2,2′-azobisisobutyronitrile (AIBN) afforded a mixture of monobromide **17** and dibromide **18** in a 92:8 ratio and 65% yield. However, bromination with 2.5 equiv of NBS afforded a separable mixture of dibromide **18** and tribromide **19** in 87:13 ratio and 75% yield. Chiral dioxinone **21** was best prepared, in racemic form, by refluxing the commercially available dioxinone **20** and pivaldehyde[19] in mesitylene for 1 h. Bromination[18] of **21** (NBS 2 equiv, sun lamp, benzoyl peroxide) provided a single product (**22**) in 70% yield. Dioxinones **23** and **24** were prepared in racemic form upon treatment of *tert*-butyl acetoacetate with isopropyl methyl ketone or acetophenone, respectively, under acidic conditions (H_2SO_4, Ac_2O), following a literature procedure.[20] Bromination of **23** and

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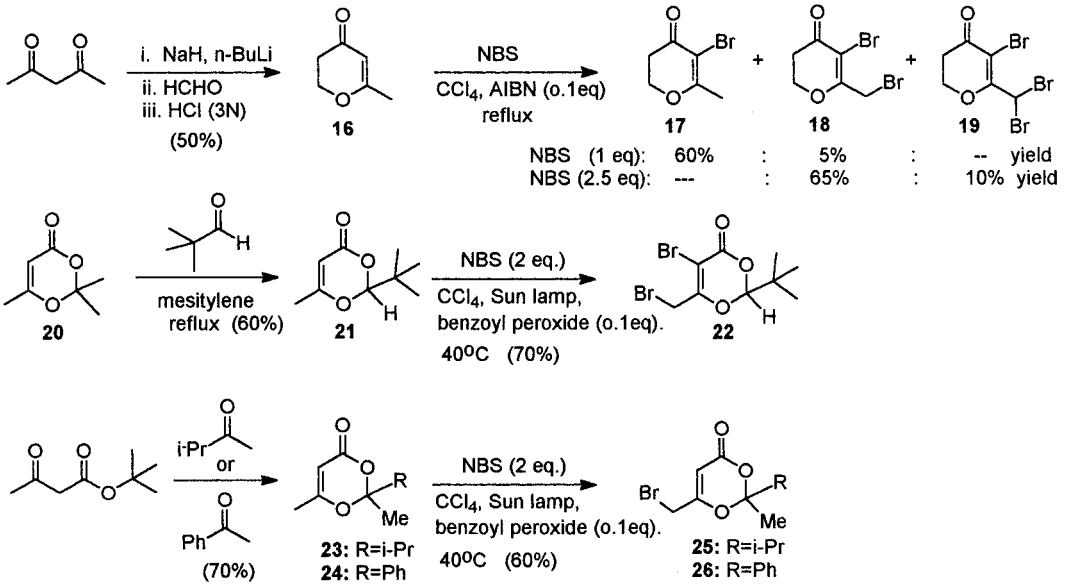
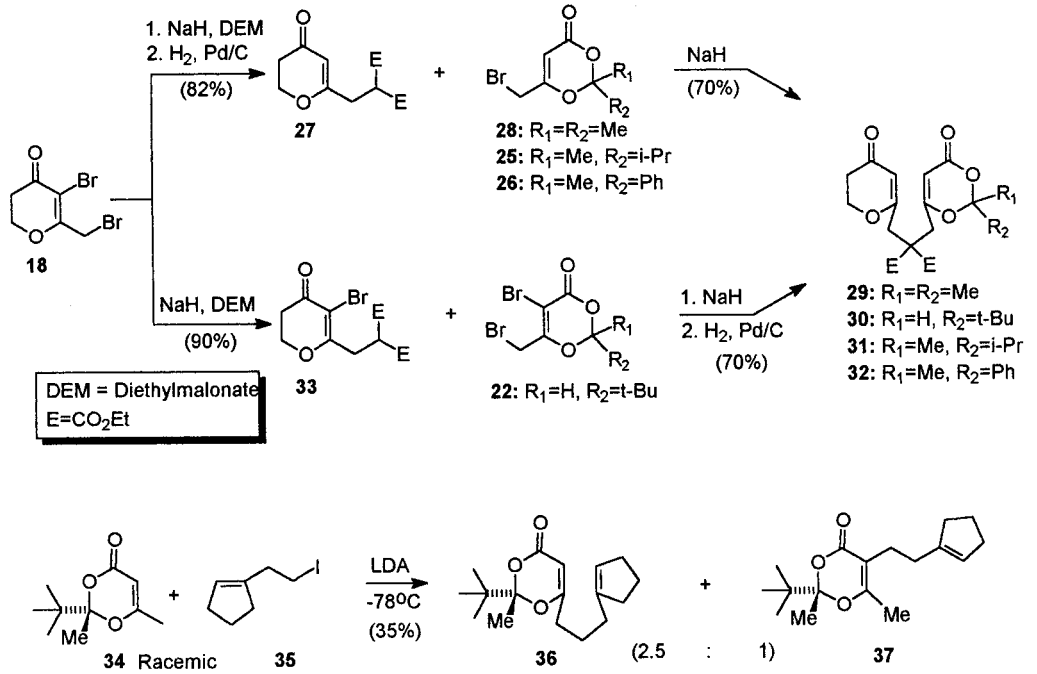
Scheme 4



Scheme 5

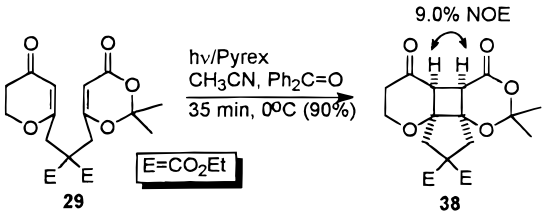


24 afforded the corresponding monobromides **25** and **26** in 60% yield.

Photosubstrates **29**, **31**, and **32** were prepared by coupling of **18** with diethyl malonate, followed by reductive cleavage of the vinyl bromide then coupling of the corresponding product (**27**) with the bromodioxinones **28**, **25**, and **26**, respectively, as described in Scheme 5. Photosubstrate **30** was prepared by coupling of dihydropyrone **33** with dioxinone **22** followed by reductive cleavage of the vinyl bromides by catalytic hydrogenation.[21] Compound **36** was prepared by coupling of dioxinone **34** with iodide **35**[22] following a previously described procedure.[9]

Examination of the Synthetic Sequence. The utility of the synthetic sequence, described in the retrosynthetic Scheme 2, was first examined with the achiral photosubstrate **29**. Compound **29** possesses two different chromophores, the dihydropyrone and the dioxinone. The former undergoes intramolecular photocycloaddition to alkenes upon direct irradiation *via* a Pyrex glass filter ($\lambda > 295$),[10] whereas photocycloaddition of

Scheme 6



(20) (a) Sato, M.; Ogasawara, H.; Oi, K.; Kato, T. *Chem. Pharm. Bull.* **1983**, *31*, 1896. (b) Huckin, S.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.

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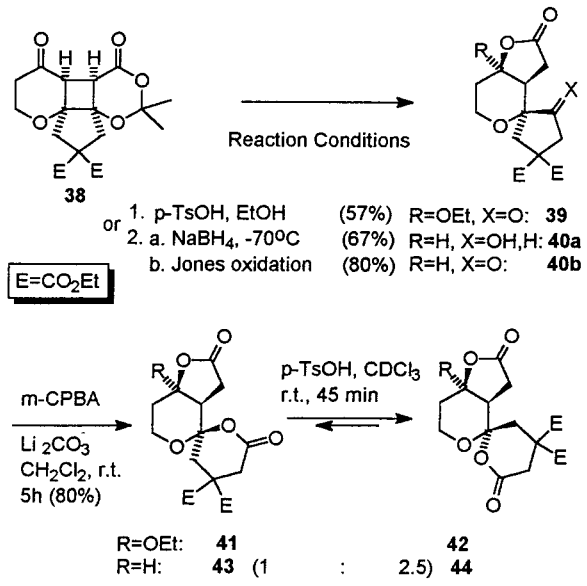
(22) (a) Corey, E. J.; Udea, Y.; Ruden, R. A. *Tetrahedron Lett.* **1975**, *16*, 4347. (b) Millar, J. G.; Underhill, E. W. *J. Org. Chem.* **1986**, *51*, 4726.

Scheme 7



dioxinones to alkenes requires a triplet sensitizer such as acetone, acetophenone, or benzophenone.[9] In contrast to the intramolecular photocycloaddition of dihydropyrones to alkenes, no photoreaction could be detected upon irradiation of **23** for several hours (over 10 h). However, highly efficient photocyclization was obtained upon irradiation of **29** in the presence of benzophenone as triplet sensitizer, providing a single product **38** in over 90% isolated yield. A 9% NOE enhancement in each of the proton signals on the produced four-membered ring, obtained upon irradiation of its vicinal proton resonance, allowed assignment of the *syn* stereochemistry. The failure of the photocycloaddition in the absence of triplet sensitizer could be attributed to efficient quenching of the electronically excited dihydropyrone by the dioxinone chromophore.

Selective cleavage of the cyclobutane ring in **38** was achieved upon treatment with hydrochloric acid in ethanol solution,[23] affording spiro ether **39** in a 57% isolated yield. The produced ketone functionality is needed for the oxidative enlargement as described in the retrosynthetic analysis (Scheme 2). The produced lactone prohibits any possible epimerizations of this part during the subsequent step of oxidative enlargement of the spiro ketone, planned for the preparation of spiro ketal structures, and allows accurate detection of epimerization at the spiro center during the oxidation step. Baeyer−Villager oxidation[24] of **39** provided a single product **41** in 80% yield with no detectable amount of is corresponding epimer **42** by ^{1}H-NMR.

The structure of **41** was determined by NMR experiments[25] and confirmed by X-ray analysis. The preferred conformation of the spiro structure possesses two axial C−O bonds at the spirocenter. The utility of this synthetic method in selective preparation of a thermodynamically less stable spiro ketal structures was demonstrated in a stereoselective synthesis of spiro ketal **43**. Epimerization of the spiro center of **43** will afford R = H at the axial position in the corresponding structure **44** instead of the axial oxygen at the lactone moiety in **43**, leading to a thermodynamically more stable isomer. Stereoselective synthesis of spiro ketal **43** (R = H) was achieved as follows: Reduction of the photoproduct **38** with $NaBH_4$ took place at the cyclic ketone with high selectivity of approach from the convex face, leading to the expected[23] spontaneous formation of the corresponding lactone *via* fragmentation of the cyclobutane ring, introducing the ketone functionality at the cyclopentane ring which was over reduced under the reaction conditions to the corresponding alcohol **40a**. Jones oxidation[26] of this alcohol afforded **40b** in 60% total yield from **38**. Baeyer−Villager oxidation of **40b** afforded a single compound **43** in 80% yield. Controlled epimerization of the spiro center was performed by treatment of **43** with p-TsOH in the presence of 4-*tert*-butylcyclohexanone as an internal standard (IS). This experiment led to clean and rapid isomerization, affording a mixture of **43** and **44** in a 1:2.5 ratio.[27] This result demonstrates the utility of the developed sequence in the preparation of thermodynamically less stable spiro ketals. Enantioselective synthesis of spiro ketals should be possible following this method upon irradiation of optically pure chiral dioxinones. High stereofacial selectivity in the intramolecular photocycloaddition of chiral dioxinones is essential in the enantioselective synthesis of spiro structures.

Enantioselective Synthesis of Spiro Structures via Photocycloaddition of Chiral Dioxinones. The demonstrated synthetic utility of the photocycloaddition of cyclic enones to alkenes in organic synthesis[28] and the absence of information on the *intramolecular* photocycloaddition of alkenes, connected to the C(β) position of the chiral dioxinones, triggered systematic investigation of the steric effect of substituents at the chiral dioxinone and/or the alkenyl side chain on the diastereofacial selectivity of this reaction. Recently, we have shown[9] that photocycloaddition of **45** at 0 °C afforded **46** and **47** in a 1:2 ratio (Scheme 8). The major product (**47**) was formed by approach of the dioxinone from the more exposed side (equatorial *tert*-butyl group), and the stereoselectivity was increased to 1:4 upon irradiation of **45** at −70 °C.

Increasing the steric hindrance at the alkenyl side chain was expected to affect the diastereofacial selectivity.[9] This was examined by the photocycloaddition of **36** at 0 °C and −70 °C, which resulted in this case in decreasing the facial selectivity to a 1:1 mixture of **48** and **49** at both temperatures. These results suggest the preferred facial selectivity from the opposite side of the *tert*-butyl substituent upon decreasing the steric hindrance of the pseudo-axial substituent at the acetal center of the chiral dioxinone. Moreover, high selectivity from the pseudo-equatorial substituent could be expected upon replacing the *tert*-butyl substituent with a less

(23) (a) Winkler, J. D.; Hershberger, P. M. *J. Am. Chem. Soc.* **1989**, *111*, 4852. (b) Winkler, J. D.; Hershberger, P. M.; Spiringer, J. P. *Tetrahedron Lett.* **1986**, *27*, 5177.

(24) For an example of selective Baeyer−Villager oxidation, see: (a) Shishido, K.; Takahashi, K.; Fukumoto, K. *J. Org. Chem.* **1987**, *52*, 5704. (b) Baldwin, S. W.; Wilkinson, J. M. *Tetrahedron Lett.* **1979**, *20*, 2657.

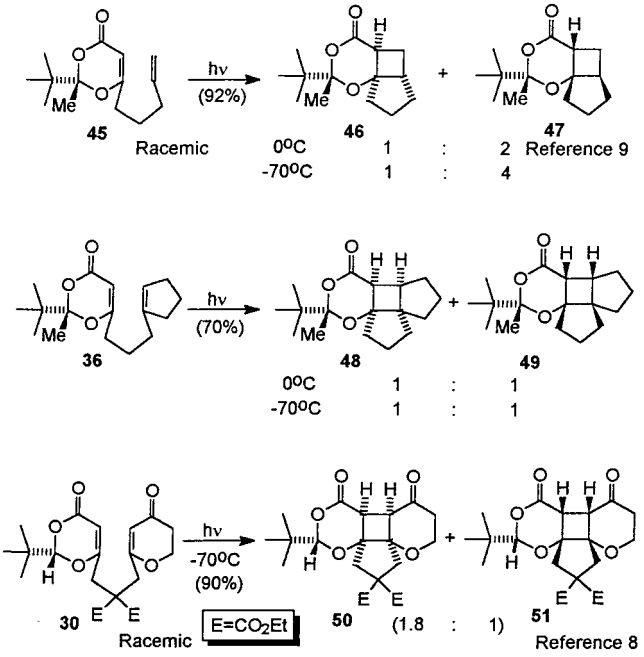
(25) The relative stereochemical relationship of the stereogenic centers was determined by NOE difference. Determination of these protons resonances carried out by COSY-45, XH-CORR, and JMOD-XH methods and was supported by NOE experiments.

(26) Brown, H. C.; Garg, C. P.; Liu, K. T. *J. Org. Chem.* **1971**, *36*, 387.

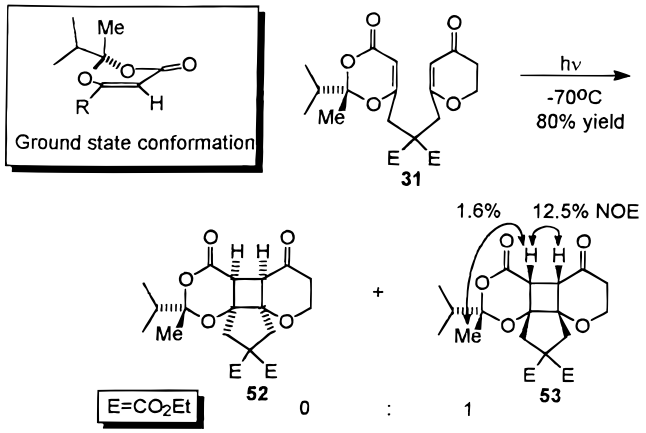
(27) The isomeric ratio was determined by ^{1}H-NMR.

(28) (a) Haddad, N. *The Chemistry of Functional Groups, Supplement A3: The Chemistry of Double-bonded Functional Groups*; Patai, S., Eds.; Wiley: New York, 1997; Chapter 13, p 641. (b) Schuster, D. I.; Lem, G.; Caprinidis, N. A. *Chem. Rev.* **1993**, *93*, 3. (c) Demuth, M.; Mikhail, G. *Synthesis 1989*, 145. (d) Becker, D.; Haddad, N. *Organic Photochemistry*; Padwa, A., Ed.; Dekker press: New York, 1989; Vol. 10, 1. (e) Crimmins, M. T. *Chem. Rev.* **1988**, *88*, 1453.

Scheme 8



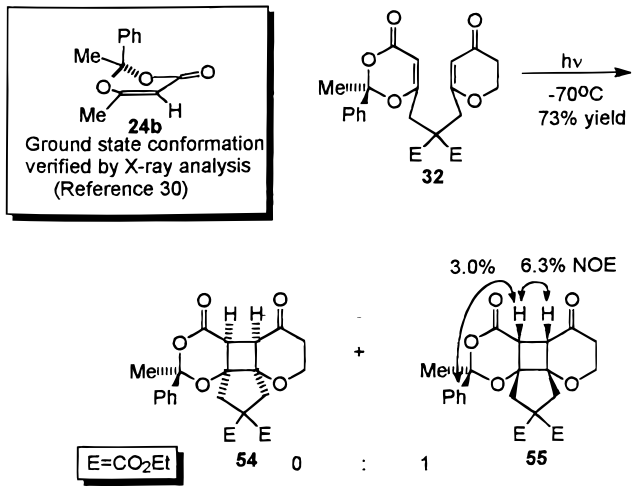
Scheme 9



sterically hindered one. The first possibility was examined by the photocycloaddition of **30** at −70 °C, which afforded a mixture of **50** and **51** in a 1.8:1 ratio and 90% yield. The preferred stereofacial selectivity was obtained from the hydrogen side of the acetal center. On the basis of the above assumption, we have anticipitated high selectivity in the cycloaddition of a chiral dioxinone possessing isopropyl and methyl substituents, from the isopropyl side.

Irradiation of **31**, possessing a methyl and isopropyl substituent, was examined under the usual conditions at −70 °C. A single product (**53**) was obtained in 80% isolated yield, with no detectable amount of the corresponding diastereomer **52**. The structure of **53** was determined by NMR.[25,29] A 12.5% NOE enhancement between the proton resonances of the four-membered ring, allows assignment of the *syn* stereochemistry. NOE enhancement between the methyl substituent at the ketal center and the cyclobutyl protons resonances, summarized in Scheme 9, allowed unambiguous determination of facial selectivity from the isopropyl side. This

Scheme 10



result is consistent with our above assumptions and provides unprecedented high facial selectivity in the intramolecular photocycloadditions of chiral 1,3-dioxin-4-ones to alkenes connected at the C(β) position of the dioxinone.

Another example of high stereofacial selectivity was obtained in the photocycloaddition of **32** from the methyl side. Irradiation of **32** at −70 °C afforded a single product **55** in 73% isolated yield, with no detectable amount of the corresponding diastereomer **54**. The key NOE enhancements, summarized in Scheme 10, allowed assignment of the stereogenic centers in **55**. Interestingly, the selectivity is consistent with the conformation of the chiral dioxinone **24b** in the crystal structure[30] and could suggest a similar orientation of the phenyl and methyl substituents in the active triplet excited state of **32**.

Epimerization of the dioxanone ketal center in photoproducts **53** and **55** was examined by treatment with oxalic acid, camphorsulfonic acid, and *p*-toluenesulfonic acid, which led to efficient epimerization in similar compounds.[9] However, treating **53** and **55** under these conditions, failed to provide a significant amount of the less stable epimers **52** and **54**, respectively, and resulted in a mixture of undefined products.

The high stereofacial selectivity obtained in the photocycloaddition of **31** and **32** allows enantioselective synthesis of spiro ethers and spiro ketals, starting from optically pure dioxinones **23** and **24** (Scheme 4) or their enantiomers. The desired optically pure dioxinones could be prepared from (*R*)-hydroxybutanoic acid[31] or (*S*)-hydroxybutanoic acid,[32] following literature procedures.[33]

Experimental Section

THF was distilled from the potassium benzophenone ketyl, and HMPA was distilled over CaH_2. Silica gel 60 (230−400 mesh ASTM) for column chromatography was used. Melting

(29) For determination of similar structures by NMR, c.f.: (a) Becker, D.; Haddad, N. *Tetrahedron* **1993**, *49*, 947. (b) Becker, D.; Haddad, N. *Isr. J. Chem.* **1989**, *29*, 303.

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points are uncorrected. EI-HR-MS spectra were recorded on a Varian Matt-71.

2-Methyl-5,6-dihydro-4*H*-pyran-4one (16). A solution of acetylacetone (10 g, 0.1 mol) in THF (20 mL) was added dropwise to a cold (0 °C) suspension of sodium hydride (0.12 mol, 3.6 g) in HMPA (15 mL) and THF (150 mL) mixture. The reaction was stirred for 20 min, then a 2.5 M solution of n-BuLi in hexane (0.12 mol, 48 mL) was introduced in a dropwise addition. The resulted mixture was stirred for 30 min, then dry paraformaldehyde powder (0.2 mol, 6 g) was added in a one portion. The reaction mixture was stirred vigorously for an additional 2 h at rt and treated with HCl (3 M, ~150 mL) until pH = 2 was reached. The resulted mixture was stirred 2.5 h, and the aqueous layer was separated and then extracted with diethyl ether. The organics were combined, washed with brine, dried over Na_2SO_4, and then concentrated under reduced pressure. Purification of the residue by flash chromatography (hexane/EtOAc = 4:1, R_f = 0.2) afforded 5.6 g of dihydropyrone **16** in 50% yield: ^{1}H-NMR ($CDCl_3$) δ 5.30 (s, 1H), 4.42 (t, J = 6.8 Hz, 2H), 2.47 (t, J = 6.8 Hz, 2H), 1.97 (s, 3H).

3-Bromo-2-(bromomethyl)-5,6-dihydro-4*H*-pyran-4-one (18). A mixture of 2-methyl-5,6-dihydro-4H-pyran-4-one (1.0 g, 8.93 mmol), NBS (1.9 g, 11.2 mmol), and AIBN (40 mg) in 30 mL of CCl_4 was refluxed for 2.5 h, and additional amounts of NBS (1.5 g) and AIBN (2 × 40 mg) were added at 1 h intervals. The reaction mixture was stirred for an additional 30 min, cooled to 0 °C, filtered, and then concentrated under reduced pressure to afford **18** and **19**. Separation of the products by flash chromatography [hexane/EtOAc 10:1; R_f (**18**) = 0.2, R_f (**19**) = 0.25] afforded 1.57 g of **18** (65% yield) and 312 mg of 19 (10% yield).

18: ^{1}H-NMR ($CDCl_3$) δ 4.55 (t, J = 8.2 Hz, 2H), 4.21 (s, 2H), 2.8 (t, J = 8.2 Hz, 2H); HR-MS calcd for $C_6H_6O_2Br_2$ m/z 269.8714, 270.8793, 271.8694; found m/z 269.8685, 270.8828, 271.8685, respectively.

19: ^{1}H-NMR ($CDCl_3$) δ 6.78 (s, 1H), 4.68 (t, J = 6.8 Hz, 2H), 2.87 (t, J = 6.8 Hz, 2H). **3-Bromo-2-methyl-5,6-dihydro-4*H*-pyran-4-one (17)** was obtained in 60% isolated yield following the above procedure, using 1 equiv of NBS: ^{1}H-NMR ($CDCl_3$) δ 4.45 (t, J = 6.8 Hz, 2H), 2.70 (t, J = 6.8 Hz, 2H), 2.25 (s, 3H); HR-MS calcd for $C_6H_7O_2Br$ m/z 189.9730, 191.9733; found m/z 189.9629, 191.9609, respectively.

2-*tert*-Butyl-6-methyl-1,3-dioxin-4-one (21). A solution of the dioxinone **20** (213 mg, 1.5 mmol) and pivaldehyde (387 mg, 4.5 mmol) in mesitylene (3 mL) was stirred under reflux for 1 h. The reaction mixture was concentrated under reduced pressure and then the crude mixture was purified by flash chromatography (hexane/EtOAc = 7:1, R_f = 0.3) to give 190 mg of the desired product in 60% yield: ^{1}H-NMR ($CDCl_3$) δ 5.26 (s, 1H), 5.02 (s, 1H), 2.02 (s, 3H), 1.04 (s, 9H).

Preparation of Dioxinones 23 and **24 (General Procedure).** Concentrated sulfuric acid (1.63 mL, 0.03 mol) was added dropwise to a cold solution (−10 °C) of *tert*-butyl acetoacetate (0.03 mol, 5 mL) and the corresponding ketone (0.06 mol) in acetic anhydride (10 mL). The mixture was stirred for 15 h at 0 °C and then carefully transferred to an ice-cooled saturated solution of potassium carbonate (~70 mL) and stirred for 30 min at room temperature. The aqueous layer was separated and extracted with chloroform (3 × 50 mL), and the organic layers were combined, washed with brine, dried over $MgSO_4$, and then concentrated under reduced pressure. Purification by flash chromatography afforded the desired dioxinone in 65−75% yield.

2-Isopropyl-2,6-dimethyl-1,3-dioxin-4-one (23) was obtained as described above in 75% yield from isopropyl methyl ketone: ^{1}H-NMR ($CDCl_3$) δ 5.17 (s, 1H), 2.20 (m, 1H), 1.95 (s, 3H), 1.53 (s, 3H), 1.01 (d, J = 1.4 Hz, 3H), 0.98 (d, J = 1.4 Hz, 3H); HR-MS calcd for $C_9H_{14}O_3$ m/z 170.0943, found m/z 170.0942.

2,6-Dimethyl-2-phenyl-1,3-dioxin-4-one (24) was obtained as described above in 65% yield from acetophenone: ^{1}H-NMR ($CDCl_3$) δ 7.42 (m, 5H), 5.14 (s, 1H), 1.99 (s, 3H), 1.86 (s, 3H).

Bromination of Dioxinones 21, 23, and 24 (General Procedure). A suspension of NBS (26.6 mmol, 4.74 g), benzoyl peroxide (1.33 mmol, 0.32 g), and the corresponding dioxinone (13.3 mmol) in dry CCl_4 (60 mL) was irradiated by sun lump and stirred at 40 °C for 4−5 h (followed by TLC). The reaction mixture was cooled down to 0 °C, filtered through Celite, and then concentrated under reduced pressure, the crude product was purified by flash chromatography to afford the desired product in 50−60% yield.

5-Bromo-6-(bromomethyl)-2-*tert*-butyl-1,3-dioxin-4-one (22) was prepared from **21** as described above, using 2.5 equiv of NBS: ^{1}H-NMR ($CDCl_3$) δ 5.14 (s, 1H), 4.18 (dd, 2H), 1.10 (s, 9H).

6-(Bromomethyl)-2-isopropyl-2-methyl-1,3-dioxin-4-one (25) was prepared from **23** as described above: ^{1}H-NMR ($CDCl_3$) δ 5.48 (s, 1H), 3.87 (s, 2H), 2.25 (m, 1H), 1.59 (s, 3H), 1.07 (d, J = 1.3 Hz, 3H), 1.03 (d, J = 1.3 Hz, 3H); HR-MS calcd for $C_9H_{13}O_3Br$ m/z 248.0014, 250.0004, found m/z 248.0011, 250.0002 respectively.

6-(Bromomethyl)-2-methyl-2-phenyl-1,3-dioxin-4-one (26) was prepared from **24** as described above: ^{1}H-NMR ($CDCl_3$) δ 7.52 (m, 2H), 7.37 (m, 3H), 5.43 (s, 1H), 3.87 (dd, J = 10.9 Hz, 2H), 1.92 (s, 3H).

2-(2,2-Dicarbethoxyethyl)-5,6-dihydro-4*H*-pyran-4-one (27). A solution of diethyl malonate (0.54 g, 3.4 mmol) in THF (2 mL) was added dropwise to a suspension of sodium hydride (0.13 g, 4.26 mmol) in THF (30 mL). The reaction mixture was stirred under reflux for 15 min and cooled to room temperature, then dibromide **18** (0.77 g, 2.84 mmol) was added, and the mixture was stirred at room temperature for additional 2 h, quenched by addition of saturated aqueous solution of $NaHCO_3$, extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography afforded 0.77 g of 3-bromo-2-(2,2-dicarbethoxyethyl)-5,6-dihydro-4*H*-pyran-4-one (**33**) in 77% yield: ^{1}H-NMR ($CDCl_3$) δ 4.48 (t, 2H), 4.2 (q, 4H), 3.72 (t, 1H), 3.21 (d, 2H), 1.28 (t, 6H). Bromopyrone **33** (1.0 g, 3.11 mmol) was added to a suspension of 40 mL of THF, 1.2 equiv of Et_3N, and 10% Pd/C (200 mg) under atmospheric pressure of H_2 at room temperature. The reaction was completed after 20 min. Filtration of the catalyst then concentration of the filtrate under reduced pressure afforded the crude product which was purified by flash chromatography (hexane/EtOAc 1:1, R_f = 0.4) to give 0.65 g of the desired product (**27**) in 90% yield: ^{1}H-NMR ($CDCl_3$) δ 5.34 (s, 1H), 4.43 (t, J = 6.9 Hz, 2H), 4.2 (m, 4H), 3.66 (t, J = 8.3 Hz, 1H), 2.37 (d, J = 8.3 Hz, 2H), 2.5 (t, J = 6.5 Hz, 2H), 1.28 (t, 6 H); HR-MS calcd for $C_{13}H_{18}O_6$ m/z 270.1103, found m/z 270.1112.

2,2-Dimethyl-6-[2,2-dicarbethoxy-3-[2-(5,6-dihydro-4-oxo-4*H*-pyran)yl]propyl]-1,3-dioxin-4-one (29). Photosubstrate **29** was prepared by coupling of dihydropyrone **27** (580 mg, 2.16 mmol) with bromodioxinone **28** (720 mg, 3.24 mmol) following the procedure described for the preparation of **33**. Purification of the crude product by flash chromatography afforded 0.6 g of the desired product as a white powder in 68% yield: mp 112−114 °C; ^{1}H-NMR ($CDCl_3$) δ 5.32 (s, 1H), 5.30 (s, 1H), 4.38 (t, J = 8.5 Hz, 2H), 4.18 (q, J = 7.2 Hz, 4H), 2.95 (s, 2H), 2.89 (s, 2H), 2.51 (t, J = 8.4 Hz, 2H), 1.63 (s, 6H), 1.25 (t, J = 7.3 Hz, 6H); HR-MS calcd for $C_{22}H_{30}O_9$ m/z 438.1890, found m/z 438.1850.

2-*tert*-Butyl-6-[2,2-dicarbethoxy-3-[2-(5,6-dihydro-4-oxo-4*H*-pyran)yl]propyl]-2-methyl-1,3-dioxin-4-one (30). Photosubstrate **30** was prepared by coupling of dihydropyrone **33** (200 mg, 0.66 mmol) with dibromodioxinone **22** (229 mg, 0.73 mmol) following the procedure described for the preparation of **33**. Purification of the crude product by flash chromatography afforded 310 mg of the corresponding dibromoproduct in 79% yield: ^{1}H-NMR ($CDCl_3$) δ 5.32 (s, 1H), 5.06 (s, 1H), 4.42 (t, 2H), 4.18 (q, 4H), 3.42 (d, 2H), 2.96 (d, 2H), 2.50 (t, 2H), 1.25 (t, 6H), 1.01 (s, 9H).

Reduction of the vinyl bromides, following the procedure described for the preparation of **27**, and then purification of the crude product by flash chromatography afforded 171 mg of the desired product as a white powder in 75% yield: mp 89−91 °C; ^{1}H-NMR (C_6D_6) δ 5.37 (s, 1H), 5.26 (s, 1H), 4.66 (s, 1H), 3.91 (m, 6H), 3.53 (t, J = 7.0 Hz, 2H), 3.00−2.8 (m, 4H), 1.93 (t, J = 7.0 Hz, 2H), 0.89 (t, 3H), 0.88 (s, 9H), 0.87 (t, 3H); HR-MS calcd for $C_{22}H_{30}O_9$ m/z 438.1890, found m/z 438.1850.

2-Isopropyl-2-methyl-6-[2,2-dicarbethoxy-3-[2-(5,6-dihydro-4-oxo-4*H*-pyran)yl]propyl]-1,3-dioxin-4-one (31). Photosubstrate **31** was prepared by coupling of dihydropyrone **27** (270 mg, 1.0 mmol) with bromodioxinone **25** (247 mg, 1.1 mmol) following the procedure described for the preparation of **33**. Purification of the crude product by flash chromatography afforded 326 mg of the desired product as a white powder in 75% yield: mp 95−97 °C; ^{1}H-NMR ($CDCl_3$) δ 5.32 (s, 1H), 5.27 (s, 1H), 4.38 (t, 2H), 4.18 (m, 4H), 2.90 (m, 4H), 2.50 (t, 2H), 2.12 (m, 1H), 1.55 (s, 3H), 1.25 (t, 6H), 1.00 (d, 6H); CI-MS [M + H] 439.1, calcd for $C_{22}H_{30}O_9$ *m/z* 438.19.

2-Methyl-2-phenyl-6-[2,2-dicarbethoxy-3-[2-(5,6-dihydro-4H-pyran)yl]propyl]-1,3-dioxin-4-one (32). Photosubstrate **32** was prepared by coupling of dihydropyrone **27** (270 mg, 1.0 mmol) with bromodioxinone **26** (311 mg, 1.1 mmol) following the procedure described for the preparation of **33**. Purification of the crude product by flash chromatography afforded 330 mg of the desired product as a white powder in 70% yield: mp 89−91 °C; ^{1}H-NMR ($CDCl_3$) δ 7.36 (m, 2H), 7.24 (m, 3H), 5.25 (s, 1H), 5.23 (s, 1H), 4.35 (m, 2H), 4.20 (m, 4H), 2.92 (m, 4H), 2.50 (m, 2H), 1.84 (s, 3H), 1.25 (m, 6H); CI-MS [M + H] 473.0, calcd for $C_{25}H_{28}O_9$ *m/z* 472.17.

2-Cyclopentenyl-1-iodoethane (35) was prepared from 2-cyclopentenylethan-1-ol[22a] in 70% yield, following Millar's procedure:[22b] ^{1}H-NMR ($CDCl_3$) δ 5.44 (s, 1H), 3.25 (t, 2H), 2.68 (t, 2H), 2.26 (m, 4H), 1.89 (m, 2H).

2-*tert*-Butyl-2-methyl-6-[3-(1-cyclopentenyl)propyl]-1,3-dioxin-4-one (36). LDA in THF solution was prepared by dropwise addition of n-BuLi (0.9 mL, 2.3 mmol, 2.5 M in hexane) to a solution of diisopropylamine (0.3 mL, 2.2 mmol) and HMPA (0.6 mL) in THF (8 mL), cooled to −70 °C. The mixture was stirred for 30 min at the same temperature to ensure complete formation of LDA. Solution of dioxinone **34** (357 mg, 1.94 mmol) in THF (3 mL) was added dropwise over a 20 min period. After the mixture was stirred for additional 45 min at −70 °C, alkenyl iodide **35** (460 mg, 2.13 mmol) in THF (2 mL) was added dropwise, then the temperature was slowly raised to room temperature over 1 h period and the resulted red solution was stirred for an additional 40 min. The reaction quenched by addition of 10% HCl (4 mL) and extracted with ether (3 × 10 mL). The combined organics were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by flash chromatography afforded the desired product **36** (154 mg) and its corresponding C(α) isomer **37** (62 mg) in 40% total yield.

Photosubstrate 36: ^{1}H-NMR ($CDCl_3$) δ 5.31 (s, 1H), 5.11 (s, 1H), 2.14 (m, 8H), 1.81 (m, 2H), 1.65 (m, 2H), 1.54 (s, 3H), 1.03 (s, 9H); HR-MS calcd for $C_{17}H_{26}O_3$ *m/z* 278.1881, found *m/z* 278.1893.

C(α) isomer 37: ^{1}H-NMR ($CDCl_3$) δ 5.33 (s, 1H), 2.23 (m, 8H), 1.94 (s, 3H), 1.83 (m, 2H), 1.52 (s, 3H), 1.03 (s, 9H); HR-MS calcd for $C_{17}H_{26}O_3$ *m/z* 278.1881, found *m/z* 278.1840.

General Procedure for the Irradiations of Dioxinones 29−32. An 80-W mercury vapor lamp (Q-81) was used for irradiations *via* a Pyrex glass filter ($\lambda > 295$). The irradiations were carried out in a solution of benzophenone (100 mg) in 18 mL of acetonitrile (0 °C) or 50% acetone/acetonitrile as solvent (−70 °C) under a nitrogen atmosphere. The concentrations always kept below 0.05 M, and the reactions were followed by the UV absorption of the starting materials on TLC and were usually completed after 3 h at −70 °C. The solvents removed under reduced pressure and the crude photoproducts were separated by flash chromatography to afford the corresponding products, as a white solid in all cases, in 70−92% total yield.

14,14-Dicarbethoxy-6α,7α-dihydro-3,3-dimethyl-2,4,11-trioxa-5,8-dioxo-13α,15α-tetracyclo[4.9.0.0^{1,12}.0^{7,12}]pentadecane (38). Irradiation of **29** at 0 °C afforded single product **38** in 90% yield. ^{1}H-NMR ($CDCl_3$) δ 4.39 (m, 1H), 4.2 (m, 4H), 3.89 (m, 1H) 3.41 (d, J = 11.2 Hz, 1H), 3.05 (d, J = 14.6 Hz, 1H), 2.92 (d, J = 11.6 Hz, 1H), 2.66 (d, J = 14.0 Hz, 1H), 2.53 (m, 3H), 2.38 (m, 1H), 1.61 (s, 3H), 1.57 (s, 3H), 1.24 (t, 3H), 1.22 (t, 3H); HR-MS calcd for $C_{20}H_{26}O_9$ *m/z* 410.1577, found *m/z* 410.1577.

Irradiation of 30: Irradiation of **30** at −70 °C afforded mixture of **50** and **51** in a 1.8:1 ratio and 90% isolated yield. **3α-*tert*-Butyl-14,14-dicarbethoxy-6α,7α-dihydro-2,4,11-trioxa-5,8-dioxo-13α,15α-tetracyclo[4.9.0.0^{1,12}.0^{7,12}]pentadecane (50):** ^{1}H-NMR (C_6D_6) δ 4.34 (s, 1H), 4.12 (m, 1H), 4.05−3.78 (m, 4H), 3.38 (dt, J = 5.9, 11.8 Hz, 1H), 3.13 (d, J_{ab} = 9.9 Hz, 1H), 2.95 (d, J_{ab} = 9.9 Hz, 1H), 2.90 (d, J_{ab} = 13.7 Hz, 1H), 2.88 (d, J_{ab} = 13.6 Hz, 1H), 2.59 (d, J_{ab} = 13.7 Hz, 1H), 2.52 (d, J_{ab} = 13.6 Hz, 1H), 2.38 (dt, J = 3.9, 15.7 Hz, 1H), 2.01 (m, 1H), 0.93 (m, 3H), 0.87 (s, 9H), 0.83 (t, 3H); HR-MS calcd for $C_{22}H_{30}O_9$ *m/z* 438.1890, found *m/z* 438.1897. **3α-*tert*-Butyl-14,14-dicarbethoxy-6*β*,7*β*-dihydro-2,4,11-trioxa-5,8-dioxo-13*β*,15*β*-tetracyclo[4.9.0.0^{1,12}.0^{7,12}]pentadecane (51):** ^{1}H-NMR (C_6D_6) δ 4.51 (s, 1H), 3.95 (m, 4H), 3.70 (d, J = 7.7 Hz, 1H), 3.52 (d, J = 7.7 Hz, 1H), 3.42 (m, 1H), 3.08 (t, J = 11.1 Hz, 1H), 2.95 (d, J = 13.6 Hz, 1H), 2.69 (d, J_{ab} = 11.2 Hz, 1H), 2.57 (d, J_{ab} = 11.2 Hz, 1H), 2.48 (d, J = 13.8 Hz, 1H), 2.38 (m, 1H), 1.77 (bd, J = 15.5 Hz, 1H), 0.91 (m, 6H), 0.86 (s, 9H); CI-MS [M+H]: 439.2; HR-MS calcd for $C_{22}H_{30}O_9$ *m/z* 438.1890, found *m/z* 438.1910.

14,14-Dicarbethoxy-6*β*,7*β*-dihydro-3α-isopropyl-3*β*-methyl-2,4,11-trioxa-5,8-dioxo-13*β*,15*β*-tetracyclo[4.9.0.0^{1,12}.0^{7,12}]-pentadecane (53). Irradiation of **31** at −70 °C, afforded **53** in 80% isolated yield: ^{1}H-NMR ($CDCl_3$) δ 4.38 (m, 1H), 4.22 (m, 4H), 3.90 (m, 1H), 3.45 (d, J = 11.0 Hz, 1H), 3.02 (d, J = 14.5 Hz, 1H), 2.91 (d, J = 14.5 Hz, 1H), 2.69 (d, J = 12.1 Hz, 1H), 2.58−2.46 (m, 3H), 2.38 (m, 1H), 2.04 (m, 1H), 1.48 (s, 3H), 1.29−1.22 (m, 6H), 1.04 (d, J = 1.7 Hz, 3H), 1.03 (d, J = 1.7 Hz, 3H); HR-MS calcd for [M − $C_5H_{10}O$, typical fragmentation of isopropyl methyl ketone] $C_{17}H_{20}O_8$ *m/z* 352.1158, found *m/z* 352.1189; CI-MS [M + H] 438.8; calcd for $C_{22}H_{30}O_9$ *m/z* 439.19.

14,14-Dicarbethoxy-6*β*,7*β*-dihydro-3α-methyl-3*β*-phenyl-2,4,11-trioxa-5,8-dioxa-13*β*,15*β*-tetracyclo[4.9.0.0^{1,12}.0^{7,12}]-pentadecane (55). Irradiation of **32** at −70 °C afforded **55** in 73% isolated yield: ^{1}H-NMR ($CDCl_3$) δ 7.38 (m, 5H), 4.46 (m, 1H), 4.15 (m, 4H), 3.90 (m, 1H), 2.98 (d, J = 12.0 Hz, 1H), 2.76 (d, J = 12.0 Hz, 1H), 2.70 (m, 1H), 2.56 (dd, J_1 = 13.0 Hz, J_2 = 17.1 Hz, 2H), 2.48 (d, J = 14.9 Hz, 1H), 2.40 (m, 1H), 2.02 (d, J = 14.9 Hz, 1H), 1.85 (s, 3H), 1.20 (m, 6H); CI-MS [M + H] 472.9; calcd for $C_{24}H_{28}O_9$ *m/z* 472.17.

Irradiation of 36: Irradiation of **36** at 0 and −70 °C afforded a mixture of **48** and **49** in a 1:1 ratio and 70% isolated yield.

3α-*tert*-Butyl-6α,7α-dihydro-3*β*-methyl-2,4-dioxa-5-oxo-12α,14α-tetracyclo[4.9.0.0^{1,11}.0^{7,11}]butadecane (48). ^{1}H-NMR (C_6D_6) δ 2.51 (d, 1H), 2.19 (dd, J = 13.4, 6.4 Hz, 1H), 2.04 (dd, J = 10.0, 8.1 Hz, 1H), 1.96 (dd, J = 13.5, 7.3 Hz, 1H), 1.81 (m, 1H), 1.70 (m, 1H), 1.57 (m, 2H), 1.42 (m, 2H), 1.41 (s, 3H), 1.35 (m, 2H), 1.18 (m, 2H), 0.84 (s, 9H); HR-MS calcd for $C_{17}H_{26}O_3$ *m/z* 278.1881, found *m/z* 278.1881.

3α-*tert*-Butyl-6*β*,7*β*-dihydro-3*β*-methyl-2,4-dioxa-5-oxo-12*β*,14α-tetracyclo[4.9.0.0^{1},^{11}.0^{7,11}]butadecane (49): ^{1}H-NMR (C_6D_6) δ 2.39 (d, 1H), 2.37 (t, 1H), 2.10 (dd, J = 11.4, 9.5 Hz, 1H), 1.96 (dd, J = 17.1, 7.6 Hz, 1H), 1.81 (m, 1H), 1.60 (m, 1H), 1.50 (m, 2H), 1.32 (m, 4H), 1.18 (m, 1H), 1.10 (m, 1H), 1.02 (bs, 12H); HR-MS calcd for $C_{17}H_{26}O_3$ *m/z* 278.1881, found *m/z* 278.1946.

4′,4′-Dicarbethoxy-6α-ethoxy-3,7*β*-dioxa-8,2′-dioxobicyclo[4.3.0]nonane-2*β*-spiro-1′-cyclopentane (39). A solution of **38** (52.5 mg, 0.13 mmol) and a catalytic amount of p-TsOH (5 mg) in 5 mL of absolute EtOH was stirred at room temperature for 18 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography to afford 29.3 mg of the desired product in 57% yield: ^{1}H-NMR (C_6D_6) δ 4.02 (m, 2H), 3.84 (m, 2H), 3.41 (dd, J = 1.7, 18.5 Hz, 1H), 3.31 (m, 3H), 3.15 (m, 1H), 2.92 (dd, J = 1.7, 17.3 Hz, 1H), 2.53 (dd, J = 8.5, 17.4 Hz, 1H), 2.37 (d, J = 8.6 Hz, 1H), 2.32 (d, J = 13.2 Hz, 1H), 2.16 (dd, J = 5.6, 17.8 Hz, 1H), 2.01 (dd, J = 5.3, 8.5 Hz, 1H), 1.54 (dt, J = 5.1, 13.9 Hz, 1H), 1.41 (m, 1H), 0.92 (t, 6H), 0.83 (t, 3H); HR-MS calcd for $C_{19}H_{26}O_9$ *m/z* 398.1577, found *m/z* 398.1559.

4′,4′-Dicarbethoxy-3,7*β*-dioxa-8,2′-dioxobicyclo[4.3.0]-nonane-2-spiro-1′-cyclopentane (40b). Photoproduct **38** (58.0 mg, 0.142 mmol) in THF solution (0.3 mL) was added in one portion to a cold mixture (−70 °C) of $NaBH_4$ (7.5 mg, 0.2 mmol) and EtOH (0.1 mL) in THF (0.9 mL). After 25 min at this temperature, H_2O was added, the organic solvents were evaporated under reduced pressure, and then the residue was

extracted with CH_2Cl_2 (3×5 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash chromatography to afford 33.9 mg of the corresponding alcohols **40a** in 67% yield: ^{1}H-NMR ($CDCl_3$) δ 4.70 (m, 1H), 4.20 (m, 4H), 4.09 (q, J = 7.9, 14.3 Hz, 1H), 3.90 (q, J = 7.8, 16.0 Hz, 1H), 3.82 (dd, J = 5.2, 12.0 Hz, 1H), 3.62 (t, J = 11.9 Hz, 1H), 2.92 (d, J = 14.6 Hz, 1H), 2.83 (dd, J = 13.0, 17.2 Hz, 1H), 2.53 (m, 1H), 2.36 (m, 3H), 2.05 (s, 2H), 1.62 (m, 1H), 1.23 (m, 6H); HR-MS calcd for $C_{17}H_{24}O_8$ *m/z* 356.1471, found *m/z* 356.1451.

The alcohols (10 mg, 0.03 mmol) were dissolved in a 1:1 solution of EtOAc/Et_2O (2 mL), followed by addition of Jones reagent (0.03 mL) at room temperature. The mixture was stirred for 6 h and extracted with EtOAc, and the combined organics were washed with saturated aqueous solution of $NaHCO_3$, dried over $MgSO_4$, and then concentrated under reduced pressure. Purification by flash chromatography afforded 8 mg of the desired ketone (**40b**) in 80% yield: ^{1}H-NMR ($CDCl_3$) δ 4.66 (q, 1H), 4.20 (m, 4H), 3.69 (m, 1H), 3.57 (m, 1H), 3.34 (d, J = 19.8 Hz, 1H), 2.83 (d, J = 14.9 Hz, 1H), 2.64 (d, J = 19.5 Hz, 1H), 2.55 (d, J = 14.6 Hz, 1H), 2.52 (s, 2H), 1.98 (m, 1H), 1.92 (m, 1H), 1.25 (m, 7H); HR-MS calcd for [M − C_2H_5O] $C_{15}H_{17}O_7$ *m/z* 309.0974, found *m/z* 309.0978; CI-MS [M + H] 355.2; calcd for $C_{17}H_{22}O_8$ *m/z* 354.36.

Preparation of Spiro Ketals 41 and 43 (General Procedure). MCPBA (0.068 mmol) was added to a mixture of the corresponding spiro ether (**39** or **40**) (0.045 mmol) and a catalytic amount of Li_2CO_3 in CH_2Cl_2 (1.0 mL). The reaction was stirred for 5 h at room temperature, quenched by addition of 10% aqueous solution of $Na_2S_2O_4$ (0.5 mL), and extracted with $CHCl_3$ (3×5 mL), and the combined organics were washed with 10% aqueous solution of K_2CO_3 and brine and then dried over Na_2SO_4 and concentrated. Purification by flash chromatography afforded the desired product in 70−75% yield.

5′,5′-Dicarbethoxy-6α-ethoxy-3,7*β*,2′*β*-trioxa-8,3′-dioxobicyclo[4.3.0]nonane-2-spiro-1′-cyclohexane (41):[34] ^{1}H-NMR (C_6D_6) δ 3.95 (q, 2H), 3.82 (m, 2H), 3.66 (td, J = 3.6, 7.2 Hz, 1H), 3.40 (d, J = 16.6 Hz, 1H), 3.30 (m, 1H), 3.11 (m, 2H), 2.5 (dd, J = 6.2, 15.0 Hz, 1H), 2.42 (d, J = 16.1 Hz, 2H), 2.17 (d, J = 14.8 Hz, 1H), 2.12 (d, J = 14.8 Hz, 1H), 1.51 (d, J = 7.2 Hz, 1H), 1.68 (d, J = 13.8 Hz, 1H), 1.25 (td, J = 6.8, 13.0 Hz, 1H), 0.9 (m, 6H), 0.82 (t, 3H); HR-MS calcd for $C_{19}H_{26}O_{10}$ *m/z* 414.1526, found *m/z* 414.1518. **5′,5′-Dicarbethoxy-3,7*β*,2′*β*-trioxa-8,3′-dioxobicyclo[4.3.0]nonane-2-nonane-1′-cyclohexane (43):** ^{1}H-NMR (C_6D_6) δ 3.90 (q, 2H), 3.81 (m, 2H), 3.75 (t, J = 11.8 Hz, 1H), 3.59 (bs, 1H), 3.40 (d, J = 16.6 Hz, 1H), 2.93 (dd, J = 7.8, 12.0 Hz, 1H), 2.49 (d, J = 16.8 Hz, 1H), 2.40 (d, J_{ab} = 14.7 Hz, 1H), 2.24 (d, J_{ab} = 14.7 Hz, 1H), 2.23 (d, J_{ab} = 17.1 Hz, 1H), 1.82 (dd, J = 8.1, 16.0 Hz, 1H), 1.43 (bd, J = 14.5 Hz, 1H), 1.32 (dd, J = 2.1, 8.5 Hz, 1H), 1.09 (m, 1H), 0.87 (t, 3H), 0.83 (t, 3H); HR-MS calcd for $C_{17}H_{22}O_9$ *m/z* 370.1264, found *m/z* 370.1256.

5′,5′-Dicarbethoxy-3,7*β*,2′α-trioxa-8,3′-dioxobicyclo[4.3.0]-nonane-2-spiro-1′-cyclohexane (44). A catalytic amount of *p*-TsOH was added to a mixture of spiro ketal **43** (20 mg, 0.054 mmol) in CH_2Cl_2 (2 mL), then the reaction mixture was stirred at room temperature, until a constant ratio of 29:71 between the isomers **43** and **44** was achieved (45 min). Separation of the isomers by flash chromatography afforded 5.5 mg (28.5% yield) of **43** and 14.1 mg (71% yield) of **44**: ^{1}H-NMR (C_6D_6) δ 4.22 (dt, J = 6.7, 10.6 Hz, 1H), 3.92 (q, 2H), 3.84 (q, 2H), 3.36 (d, J = 16.8 Hz, 1H), 3.27 (t, J = 11.5 Hz, 1H), 2.91 (q, J = 5.2, 11.6 Hz, 1H), 2.43 (d, J = 16.8 Hz, 1H), 2.31 (d, J = 14.6 Hz, 1H), 1.90 (d, J = 14.7 Hz, 1H), 1.85 (t, J = 7.3 Hz, 1H), 1.74 (t, J = 13.2 Hz, 1H), 1.65 (dd, J = 8.6, 16.4 Hz, 1H), 1.23 (m, 2H), 0.89 (t, 3H), 0.84 (t, 3H); HR-MS calcd for $C_{17}H_{22}O_9$ *m/z* 370.1264, found *m/z* 370.1296.

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Supporting Information Available: Copies of ^{1}H-NMR spectra of all key compounds, ^{13}C-NMR spectra of **29**−**32**, **48**, and **49**, COSY-45 and selected NOE difference spectra of **38**, **41**, **43-51**, **53**, and **55**, ^{1}H-NMR spectra of the isomerization studies of **43**, and ORTEP presentation of the X-ray structure of **41** (61 pages). This material is contained in 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.

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(34) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre the coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.