Intramolecular Photochemical Dioxenone−Alkene [2 + 2] Cycloadditions as an Approach to the Bicyclo[2.1.1]hexane Moiety of Solanoeclepin A

Richard H. Blaauw, Jean-François Brière, Remco de Jong, Jorg C. J. Benningshof, Angeline E. van Ginkel, Jan Fraanje,† Kees Goubitz,† Henk Schenk,† Floris P. J. T. Rutjes, and Henk Hiemstra*

Institute of Molecular Chemistry, Laboratories of Organic Chemistry and Crystallography, University of Amsterdam, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands

henkh@org.chem.uva.nl

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A synthesis of the bicyclo[2.1.1]hexane substructure of solanoeclepin A (**1**), the most active natural hatching agent of potato cyst nematodes, was approached via an intramolecular [2 + 2] photocycloaddition. Aldehyde **12** containing the dioxenone chromophore served as a useful starting material, allowing the synthesis of a variety of photocycloaddition substrates via Grignard addition or via a Nozaki−Hiyama−Kishi reaction. Photolysis of the unsubstituted alkene **14** led to the expected crossed cycloadduct bicyclo[2.1.1]hexane **15** according to the so-called rule of five. However, several functionalized alkenes **18**, **20**, and **31** exhibited a complete reversal of cycloaddition regioselectivity, providing straight cycloadducts bicyclo[2.2.0]hexanes **21**−**26** and **4**, respectively. Their structures were proved by a combination of extensive NMR measurements, X-ray analyses, and subsequent retro-aldol reactions. The latter de Mayo process allowed the formation of spiro-[3.5]nonane **35** and spiro[3.4]octane **36** as well as the cyclobutanes **37** and **38**. Finally, the cyclization of the more rigid lactone precursor **28** occurred in high yield in the desired fashion with complete regio- and stereoselectivity to give **3** containing the core bicyclo[2.1.1]hexane skeleton of the natural product.

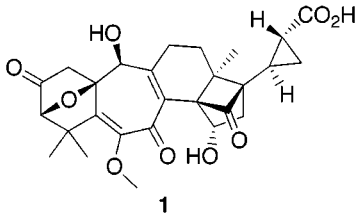
Introduction

Solanoeclepin A (**1**, Scheme 1), excreted in minute quantities by the potato root, is the most active natural hatching agent of the potato cyst nematode,[1] organisms causing severe crop losses in potato production. Its structure was elucidated in 1992 after the joint efforts of a number of research teams in The Netherlands.[2] The molecule contains all ring sizes ranging from three to seven, including a highly strained bicyclo[2.1.1]hexanone unit, which to the best of our knowledge is an unprecedented structural feature in natural products. The fascinating architecture of this novel natural product, combined with its scarcity and its potential role in the search for an environmentally benign method to combat the nematode, make it a challenging target for total synthesis.

During our first studies toward this goal,[3] the key step of our approach toward the right-hand side substructure of solanoeclepin A was based on a [2 + 2] photocycloaddition reaction (Scheme 2). We have recently reported[3a] the successful diastereoselective formation and further transformation of the highly substituted cyclobutane ring **3** starting from the lactone dioxenone precursor **2a**. Nevertheless, the cyclization process turned out to be remarkably dependent on the substitution pattern of the pendant alkenes of **2**, leading either to bicyclo[2.1.1]-hexanes of type **3** (crossed adducts) or bicyclo[2.2.0]-hexanes (straight adducts), e.g., **4**.

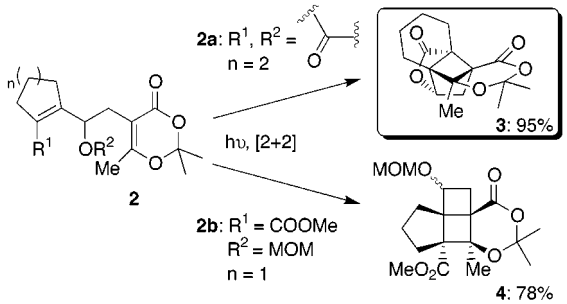
Indeed, the dioxenone structure has been frequently shown to be a versatile and efficient building block in

Scheme 1



1

Scheme 2



* Corresponding author.

† Laboratory of Crystallography.

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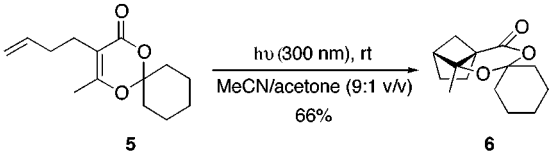
Scheme 3



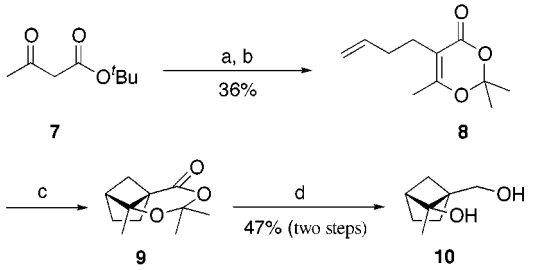
synthetic photochemistry,[4] especially allowing elegant cyclobutane ring formation via [2 + 2] cycloaddition. Moreover, in its intramolecular version, a high degree of stereo- and regiochemical control is usually attainable due to geometric contraints.[5] For instance, the photocyclization of 1,3-dioxen-4-one **5** bearing a 3-butenyl side chain at C-5 gives crossed adduct **6** (Scheme 3), as reported by Kaneko and Sato.[6a] This outcome follows the so-called empirical rule of five,[7] which explains the regiochemistry by the supposedly preferential 1,5-closure during the first step of the cyclization process. As far as we know, this is the only example of a bicyclo[2.1.1]-hexane prepared by this method. The behavior of more highly substituted alkenes in this intramolecular process with the alkene tethered at the dioxenone C-5 carbon has not been studied to the best of our knowledge.[8] However, the substitution pattern of the alkene moiety is known to govern the regioselectivity in the corresponding enone series.[5]

In conjunction with our previous work[3a] toward the synthesis of the bicyclo[2.1.1]hexane substructure of solanoeclepin A, we now report in detail our investigations of intramolecular photochemical [2 + 2] cycloadditions of several dioxenones of type **2**. Subsequently, we will outline the exploration of further chemistry of the strained bicyclohexanes obtained, including their fragmentation via retro-aldol reactions in the so-called de Mayo process.

Results and Discussion

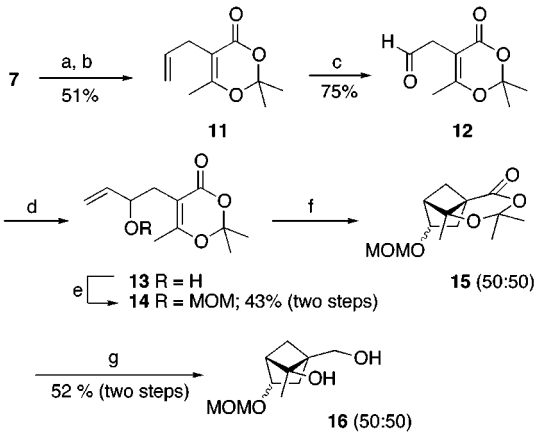
Initial Studies. Our first experiments had two objectives, viz. (1) to verify the robustness of the photocyclization process of Kaneko[6a] and (2) to establish that further transformations of the cycloadducts were possible without destruction of the fragile bicyclo[2.1.1]hexane rings.[6b] Our first photocyclization precursor was synthesized (Scheme 4) from commercially available *tert*-butyl acetoacetate **7** via alkylation with 4-bromo-1-butene and subsequent dioxenone formation according to a literature procedure leading to **8**.[9] On subjection of dioxenone **8** to irradiation at 300 nm (acetonitrile/acetone 9:1 v/v, rt), complete conversion of starting material was observed (^{1}H NMR)

Scheme 4[a]



[a] Reaction conditions: (a) 4-bromo-1-butene, KO^{t}Bu, NaI (cat), THF, 0 °C → reflux, 16 h; (b) Ac_2O, acetone, −10 °C → rt, 16 h; (c) *hν*, MeCN/acetone (9:1 v/v), rt, 3−4 h; (d) $LiAlH_4$, rt, THG, 10 min.

Scheme 5[a]



[a] Reaction conditions: (a) allyl bromide, KO^{t}Bu, NaI (cat), THF, 0 °C → reflux, 16 h; (b) Ac_2O, acetone, −10 °C → rt, 16 h; (c) OsO_4, H_2O/THF, rt, 8 h; (d) vinylmagnesium bromide, THF, −78 °C, 15 min; (e) MOMCl, $^i Pr_2NEtCH_2Cl_2$, rt, 16 h; (f) *hν*, MeCN/aceton (9:1 v/v), rt, 3−4 h; (g) $LiAlH_4$, THF, rt 10 min.

after about 4 h, and the expected 1,5-closure or crossed adduct **9** was formed. This cycloadduct appeared to be unstable, decomposing slowly under the reaction conditions and during the subsequent workup. Therefore, dioxanone **9** should be immediately reduced to diol **10**. However, the required conversion of this type of dioxanone fused with a cyclobutane ring into a 1,3-diol proved to be rather problematic. Reductions with either DIBALH or $LiAlH_4$ at temperatures ranging from −78 to 0 °C gave poor yields. We reasoned that a more rapid and exhaustive reduction was needed to circumvent these problems, which were probably resulting from a competitive retro-aldol process of the intermediate in the reduction process. Gratifyingly, reaction with excess $LiAlH_4$ at room temperature was reasonably successful and gave diol **10** as a crystalline compound in 47% overall yield from **8**. Importantly, the X-ray crystal structure determination of **10** provided unequivocal proof of the bicyclo[2.1.1]-hexane structure.

Having reached our first two objectives, we were interested to see whether similar chemistry was possible with a C-2 oxygen substituent in the 3-alkenyl side chain. Therefore, the allyl derivative **11** was synthesized in the same manner as **8** by reaction of keto-ester **7** with allyl bromide[10] (Scheme 5). The oxidative cleavage of olefin **11** by OsO_4/$NaIO_4$ allowed formation of the sufficiently

(4) Some examples of intramolecular [2 + 2] cycloadditions of dioxenones and their applications: (a) Kaneko, C.; Sato, M.; Sakaki, J.; Abe, Y. *J. Heterocycl. Chem.* **1990**, *27*, 25. (b) Winkler, J. D.; Mazur Bowen, C.; Liotta, F. *Chem. Rev.* **1995**, *95*, 2003. (c) Haddad, N.; Rukhman, I.; Abramovich, Z. *J. Org. Chem.* **1997**, *62*, 7629. (d) Winkler, J. D.; Doherty, E. M. *J. Am. Chem. Soc.* **1999**, *121*, 7425.

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(8) Sato, M.; Abe, Y.; Ohuchi, H.; Kaneko C.; Inoue, N.; Furuya, T.; Inukai, N. *Heterocycles* **1990**, *31*, 2115.

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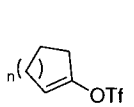
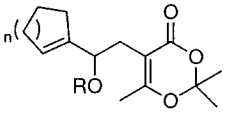
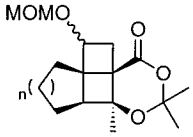
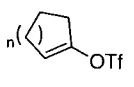
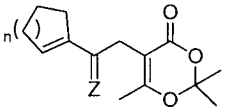
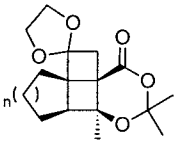
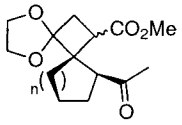
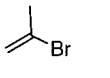
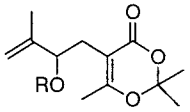
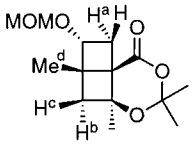
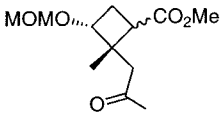
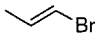
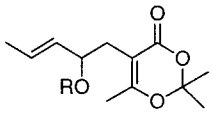
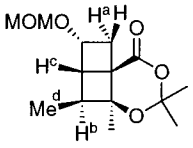
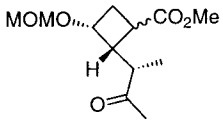
(10) Boyd, R. E.; Rasmussen, C. R.; Press, J. B. *Synth. Commun.* **1995**, *25*, 1045.

Table 1.

REACTANT + **12**	PRECURSOR preparation method (yield[c])	CYCLOADDUCT[a] time (min)	CYCLOADDUCT[a] yield (ratio)	RETRO-ALDOL PRODUCT[b] yield (ratio)
				
	R = H[d] → R = MOM			
n = 2	**17a** *e* → **18a** (73%)	<30	**21** 83% (50:50)	
n = 1	**17b** → **18b** (42%)	<30	**22** 97% (57:43)	
				
	Z = H,OH[d] → Z = O → Z = $(OCH_2)_2$			
n = 2	**17a** *f* → **19a** *g* → **20a** (54%)	90	**23** 95%	**35**[j] 75% (70:30)
n = 1	**17b** → **19b** → **20b** (33%)	60	**24** 100%[h]	**36**[j] 78% (50:50)
				
	R = H[d] → R = MOM			
	17c *e* → **18c** (69%)	120	**25** 47%	**37** 77% (70:30)
				
	R = H[d] → R = MOM			
	17d *e* → **18d** (29%)	390	**26** 36% (70:20:10)[j]	**38** 75% (70:30)[j]

[a] *hν*, MeCN/acetone. [b] KOH, dioxane/H_2O; CH_2N_2, MeOH. [c] Overall yield of the cyclization precusor from aldehyde **12**. [d] $CrCl_2$, $NiCl_2$ (cat)., DMF. [e] MOMCl, *i*-Pr_2NEt, CH_2Cl_2. [f] Swern oxidation. [g] $(TMSOCH_2)_2$, TMSOTf, CH_2Cl_2. [h] Yield of the crude product. [f] Overall yield from precursors **20a**,**b**. [j] Structure of the main adduct drawn.

stable aldehyde **12**, which served as a key intermediate in our subsequent studies (vide infra). The reaction of **12** with vinylmagnesium bromide gave **13**, thus allowing the installation of the required secondary alcohol. The alcohol was subsequently protected (**14**) with the methoxymethyl group (MOM).

The photocycloaddition of **14** (Scheme 5) gave the unstable crossed adduct **15** as a 50:50 diastereoisomeric mixture. Immediate reduction as described above led to diol **16** as a 50:50 mixture of isomers in 52% overall yield from **14**, thus establishing the feasibility of our synthetic approach to the bicyclo[2.1.1]hexane substructure of solanoeclepin A.

Expecting that this promising methodology could be extended to prepare structures of type **3**, our attention was directed to more substituted alkenes for the intramolecular photocycloaddition reaction. One additional remark about the superfluous dioxenone C-6 methyl group should be made here. The presence of this methyl group greatly facilitates the synthesis of the required dioxenones. We were aware, however, that removal of this extra carbon at a later stage of the total synthesis might not be a trivial chore.

Intramolecular [2+2] Photocycloaddition with Di- and Trisubstituted Alkenes. Aldehyde **12** served as an excellent starting material for the preparation of the photocycloaddition precursors collected in Table 1. These syntheses began with a Nozaki−Hiyama−Kishi reaction[11] (NHK) of aldehyde **12** with suitable vinylic bromides or cycloalkenyl triflates,[12] followed by MOM protection of the resulting alcohols **17** to give substrates **18**. Alternatively, the intermediate alcohols were oxidized (**19**) and subsequently converted into cyclic acetals[13] **20**, to prevent formation of mixtures of epimers at the α-carbon atom of the secondary alcohol in the subsequent photocycloaddition.

Upon irradiation of the substrates at 300 nm in an acetone/acetonitrile mixture, smooth cyclization occurred to afford cycloadducts **21**−**26** (Table 1). Surprisingly, all of these photocycloadditions proceeded with complete regioselectivity for 1,6-closure resulting in bicyclo[2.2.0]-hexanes, which are the so-called straight adducts instead of the expected crossed adducts. The structural proof of the adducts was not trivial and will be outlined in the sequel.

A readily noticed and most remarkable property of the adducts **21**−**26** was their greatly enhanced stability compared to bicyclo[2.1.1]hexanes **9** and **15**. Silica gel column chromatographic purification was possible and allowed the full characterization of these strained mol-

(11) (a) Fürstner, A. *Chem. Rev.* **1999**, *99*, 991. (b) Takai, K.; Tagashira, M.; Kuroda, T.; Ishima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.

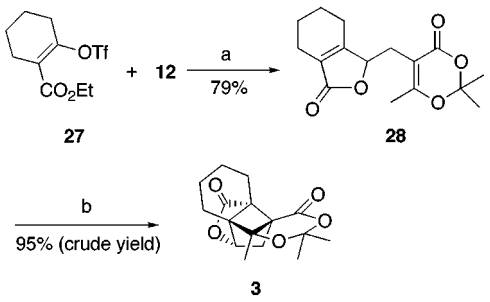
(12) Stang, P. J.; Hanack, M.; Subramania, L. R. *Synthesis* **1982**, 95.

(13) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.

ecules. Cycloalkenyl precursors **18a**, **18b**, **20a**, and **20b** reacted more efficiently than the acyclic alkenes **18c** and **18d**. Ring size had no influence on the regiochemical outcome as is apparent from comparison of the cyclohexenyl precursors with their cyclopentenyl analogues. The MOM-protected precursors **18a** and **18b** led to diastereoisomeric mixtures with low selectivity (**22**) or unselectively (**21**). Photocycloaddition of the acetals **20a** and **20b** gave the corresponding straight adducts **23** and **24**, respectively, as single products in excellent yields. Both acyclic alkene precursors **18c** and **18d** bearing a methyl group led to the adducts **25** and **26**, respectively, in moderate yields, due to partial polymerization of the precursors.[14] Product **25** appeared to be a single diastereoisomer as no other isomers in the ^{1}H NMR of the crude reaction mixture could be detected. NOE difference measurements indicated the proximity of H^a and H^b and of H^c and the proximate methyl group (Me^d) so that the relative stereochemistry of **25** could be assigned. Photolysis of **18d** proceeded more slowly than its analogue **18c** and resulted in a complex mixture, of which three inseparable diastereoisomers were obtained after column chromatography in a ratio of 70:20:10. Due to the presence of other minor adducts in the ^{1}H NMR spectrum of the crude product (minor adducts **26** <10%), which turned out to be unstable during subsequent purification, it was not possible so far to rule out the presence of small amounts of crossed adducts. However, the determination of the stereochemistry of the main isomer of **26** was possible by using NOE difference experiments in the same way as for **25**. Both adducts **25** and **26** have the protected alcohol group at the concave side and the methyl group at the convex side of the bicyclo[2.2.0]-hexane moiety. In both cases a noteworthy stereoselectivity of the reaction was observed, probably due to the more important steric interaction between the methyl group with the MOM protected alcohol in comparison with the methylene carbon in the cycloalkenyl structures.

So far, di- and trisubstituted alkenes have thus appeared reluctant to give 1,5-closure. We reasoned that the regiochemistry could perhaps be directed by stereoelectronic effects. Although not a general feature,[15] it is known that the [2 + 2] cycloaddition between an enone and an alkene bearing an electron-withdrawing group can be directed toward the formation of the cyclobutane product with head to head regiochemistry. Then, the next attempt to direct the regiochemical outcome of the [2 + 2] photocycloaddition was to use the more rigid lactone **28** (Scheme 6), which was obtained through spontaneous cyclization of the product from the NHK reaction[16] of aldehyde **12** with triflate **27**,[17] bearing an additional electron-withdrawing ester group. We were delighted to find that the cyclization of this precursor did occur in a 1,5-fashion affording the desired crossed adduct **3** as a single diastereoisomer in a clean reaction (according to ^{1}H NMR) in 95% yield of unpurified crystalline product. The adduct decomposed on a silica gel column, but could

Scheme 6[a]



[a] Reaction conditions: (a) $CrCl_2$, $NiCl_2$ (cat), DMF, 50 °C, 7 h; (b) *hν*, MeCN/acetone (9:1 v/v), rt, 2 h.

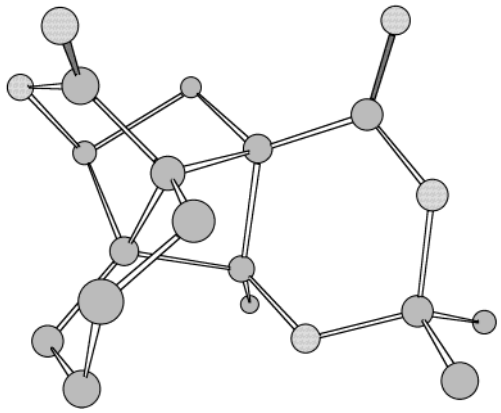
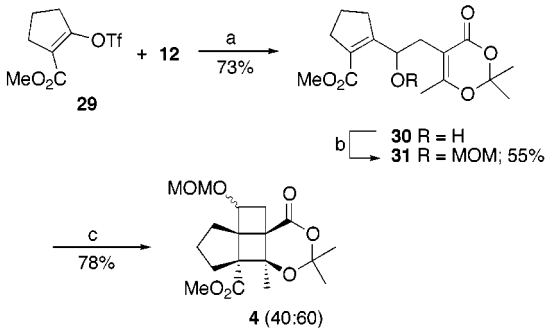


Figure 1. Chem 3D view of the crystal structure of **3**.

Scheme 7[a]



[a] Reaction conditions: (a) $CrCl_2$, $NiCl_2$ (cat), DMF, 50 °C, 18 h; (b) MOMCl, ^{i}Pr$_2$NEt, CH_2Cl_2, rt, 16 h; (c) *hν*, MeCN/acetone (9:1 v/v), rt, 1 h.

be purified by recrystallization (mp 177−178 °C). An X-ray crystal structure determination (Figure 1) proved beyond doubt that the desired cycloaddition had taken place. Comparison of the pentacyclic skeleton of **3** with the target structure **1** indicates that in an efficient five-step linear sequence from commercially available starting materials a potentially useful intermediate for the total synthesis of solanoeclepin A has been constructed.

To probe the generality of this cyclization mode, we also investigated the five-membered ring ester **31** (Scheme 7). This precursor was constructed via an NHK reaction of aldehyde **12** with triflate **29**,[18] followed again by MOM protection. With this size ring, no spontaneous lactonization of **30** was observed. Once again, the cyclization

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(15) General discussion and examples of stereoelectronic effects on the regiochemical outcome of photocycloadditions of dioxenones and enones with alkenes: (a) Fischer, E.; Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 925. (b) Sato, M.; Abe, Y.; Ohuchi, H.; Kaneko C.; Furuya, T.; Inukai, N. *Heterocycles* **1990**, *31*, 2115. (c) Andrew, D.; Hastings, D. J.; Weedon, A. C. *J. Am. Chem. Soc.* **1994**, *116*, 10870.

(16) Knochel, P.; Rao, C. J. *Tetrahedron* **1993**, *49*, 29.

(17) Piers, E.; Tse, H. L. A. *Can. J. Chem.* **1993**, *71*, 983.

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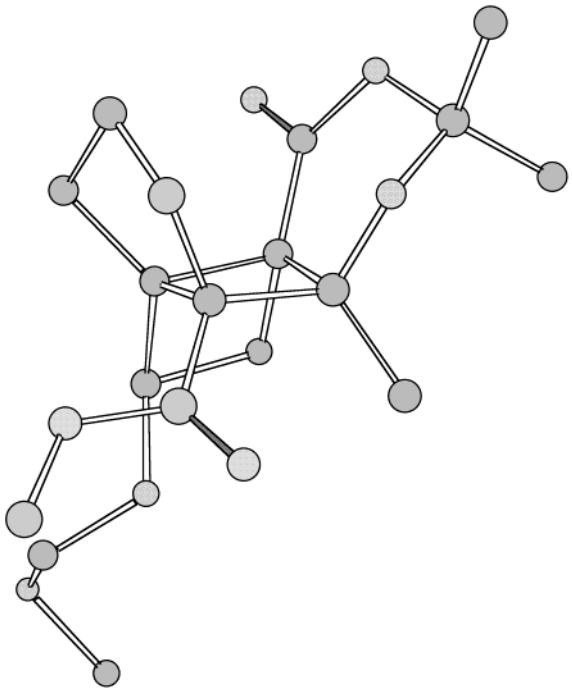

Figure 2. Chem 3D view of the crystal structure of **4** (minor isomer).

of **31** occurred exclusively with head to tail selectivity affording the straight adduct **4** as a 60:40 mixture of stereoisomers (78% yield) which was separable by flash chromatography. The minor isomer was crystalline (mp 62−64 °C) and appeared suitable for a crystal structure determination by X-ray diffraction. As shown in Figure 2 the strained tetracyclic structure is clearly the result of 1,6-closure.

Mechanistic Discussion. Thus, of the 10 photocycloaddition precursors investigated, three (**8**, **14**, and **28**) cyclize in the expected crossed mode obeying the rule of five, while the others (**18a**−**d**, **20a**,**b**, and **31**) cyclize in the unexpected straight mode. In view of the precedent available,[6a] **8** and **14** show "normal" cyclization behavior (rule of five). The mechanism of the photocycloaddition reaction of alkenes with cyclic enones has been the subject of a number of investigations.[19] The most recent experimental data on inter-[20] and intramolecular processes[21] suggest that the regiochemistry of the cyclization depends on the partitioning of the 1,4-biradical intermediate in the triplet excited state between cyclobutane ring formation and bond cleavage to give the ground state starting material as was first suggested several years ago by Bauslaugh.[22] About dioxenones much less is known.[5] In the intramolecular process, the initial bond formation should take place at the C(β) of the formed 1,4-biradical dioxanyl moiety as has been shown by Winkler et al.[23]

Keeping this in mind, preliminary modeling studies by molecular mechanics (MM2 force field)[24] indicate that in the case of cyclic alkenes **18a**,**b**, **20a**,**b**, and even with the ester **31** initial five-membered ring formation cannot

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(21) Rudolph, A.; Weedon, A. C. *Can. J. Chem.* **1990**, *68*, 1590.
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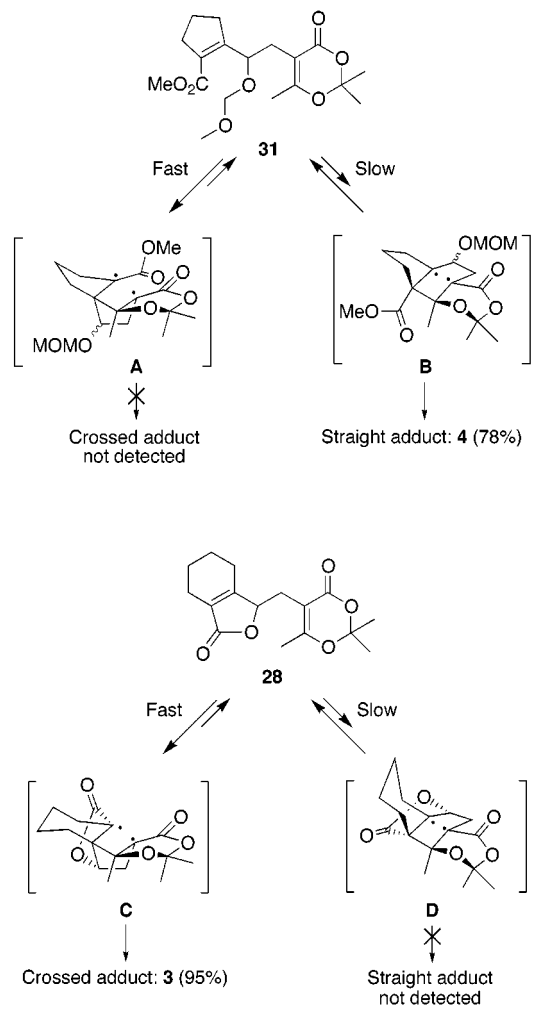
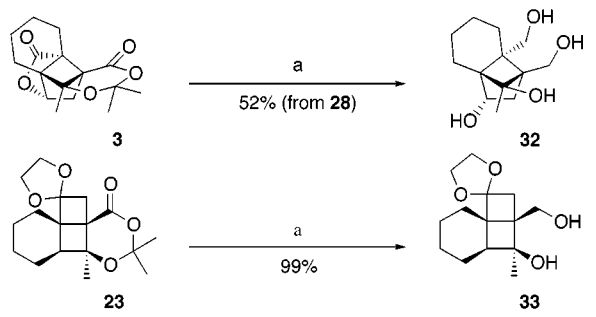
Scheme 8



be readily followed by a second CC-coupling due to conformational constraints (the two radicals are almost parallel). Therefore, the triplet 1,4-biradical intermediate **A** (Scheme 8, the biradical derived from **31** is taken as an example) would collapse back to ground state starting material. However, if biradical structure **B** is formed upon 1,6-closure, both radicals are properly oriented to allow the second CC-bond formation to occur. On the other hand, the more rigid lactone intermediate **C** puts the two radicals in a favorable orientation (productlike conformation by pyramidalization of the radical next to the lactone), allowing facile crossed adduct formation. In the case of acyclic alkenes **18c**,**d** the conformational effect is less obvious. Moreover, both low yields and slow reaction rates indicate a difficult process. One can think that the first attack on the least-hindered carbon of **18c** could justify the regiochemical outcome leading to the straight adduct. Moreover, the presence of unstable side products in the case of the analogue **18d**, of which we assume to be crossed adducts (see above), suggests that the regioselectivity is less pronounced. However, during the straight adduct formation, the second cyclization step could be favored due to the lack of the methyl group shielding the radical. At any rate, photochemistry once again proves to be a very powerful synthetic technique, producing in one step four contiguous quaternary carbon centers with complete diastereocontrol.

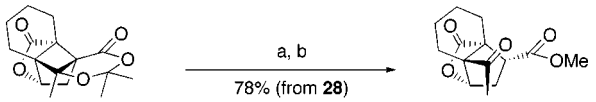
Further Reactions of the Photoadducts. We have investigated the reduction and the fragmentation of a

Scheme 9[a]



[a] Reaction conditions: (a) $LiAlH_4$, THF, rt, 5 min.

Scheme 10[a]



[a] Reaction conditions: (a) KOH, dioxane/H_2O, rt, 150 min; (b) CH_2N_2, MeOH, 0 °C.

number of the cycloadducts in order to obtain more structural proof and to probe their potential synthetic utility. First of all, cycloadduct **3** was reduced using LAH at room temperature (Scheme 9), yielding a good precursor[3a] (**32**) to construct the right-hand substructure of solanoeclepin A. Interestingly, the complete reduction of adduct **23** with LAH, as described above, proved to be extremely efficient and provided diol **33** in virtually quantitative yield.

It is well-known that a dioxanone fused to a cyclobutane can be readily fragmented via a retro-aldol reaction, providing a variation on the classical de Mayo approach. This process has found several applications in the synthesis of complex molecules.[4] The bicyclo[2.1.1]hexane **3** (Scheme 10) and bicyclo[2.2.0]hexanes **21**−**26** (Table 1) were subjected to the retro-aldol reaction under basic conditions followed by methylation with diazomethane. Thereby, the crossed adduct **3** allowed formation of the interesting tricycloundecane structure **34** as a single product. The pseudoequatorial position of the ester group was deduced from the nuclear Overhauser effect between the acetyl methyl group and the five-membered ring protons.

New functionalized cyclobutane structures **35**−**38** were obtained in good yields from the straight adducts. The cyclohexane and cyclopentane straight adducts **23** and **24** underwent ring fragmentation to spiro compounds **35** and **36**, respectively, obtained as mixtures of epimers in ca. 75% overall yield from the alkene precursors **20a** and **20b**. Because the retro-aldol reaction proceeds through an ester enolate intermediate, epimerization most probably takes place at this position. Both isomers of **35** could be separated by flash chromatography. The main epimer of **35** was a crystalline solid (mp 86 °C), which was subjected to X-ray analysis. This epimer showed the same stereochemistry as precursor **23**. More importantly, this X-ray structure ultimately proved the mode of photocycloaddition, i.e., the structure of **23**.

The retro-aldol sequence was also applied to the straight adducts **25** and **26**. Although the latter was not completely pure, both underwent clean base-induced fragmentation to **37** and **38**, respectively, as 70:30 isomeric mixtures, which were fully characterized as cyclobutanes by extensive NMR experiments. These cyclobutane products can only arise from straight adducts (a crossed adduct would lead to a five-membered ring), so that herewith the 1,6-closure process in the case of acyclic alkenes **18c** and **18d** was unequivocally proven. Finally, this de Mayo variant provides a synthetic pathway toward trifunctionalized spiro[3.5]nonanes or spiro[3.4]octanes[25] as well as to novel substituted cyclobutanes.

Conclusions

During our efforts toward the synthesis of solanoeclepin A, the construction of a variety of [2 + 2] cycloaddition precursors has been efficiently achieved. The unsubstituted olefins **8** and **14** gave the desired bicyclo[2.1.1]hexanes **9** and **15** according to the so-called rule of five. However, photocyclization of the cyclic alkenes **18a**,**b**, **20a**,**b**, and **31** and the methyl-substituted acyclic alkenes **18c**,**d** exhibited remarkable regioselectivity for 1,6-closure, leading to highly substituted bicyclo[2.2.0]hexanes **21**−**26** and **4**. Some of these cycloadducts were subjected to a retro-aldol reaction under basic conditions providing a straightforward way to polyfunctionalized cyclobutanes (**37** and **38**), also contained within spiro structures (**35** and **36**) with three or four new stereogenic centers. Photocycloaddition of the more rigid lactone precursor **28** proceeded with complete selectivity for the 1,5-mode of cyclization. This allowed the stereoselective synthesis of the highly compact and complex pentacyclic bislactone **3** in only five steps from commercially available *tert*-butyl acetoacetate. Reduction of this cycloadduct afforded **32**, which contains the appropriate substitution pattern and stereochemistry for elaboration toward the right-hand substructure of solanoeclepin A (**1**). Although the exact effects which direct the regiochemical outcome of the cycloadditions have to be further investigated, the high regioselectivity of the cyclizations described above, is noteworthy. This method provides an efficient and stereoselective approach to densely functionalized bicyclo[2.1.1]hexanes and bicyclo[2.2.0]hexanes. Application of this methodology in the total synthesis of solanoeclepin A is currently under investigation. However, to facilitate the formation of the eventual cyclobutanone functionality, an analogue of **28** lacking the methyl at C-6 of the dioxenone is now being studied. Details about these investigations will follow in due course.

Experimental Section

All reactions were carried out under an inert atmosphere of dry nitrogen, unless stated otherwise. Standard syringe techniques were applied for transfer of air-sensitive reagents and dry solvents. Infrared (IR) spectra were obtained from $CHCl_3$ solutions and wavelengths (ν) are reported in cm^{-1}. ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were determined in $CDCl_3$ (400 and 100 MHz, respectively) unless indicated otherwise. Chemical shifts (δ) are given in ppm downfield from tetramethylsilane. Chromatographic purification refers to flash chromatography[26] using the indicated solvent (mixture) and Acros silica gel (0.030−0.075 mm). R_f values were obtained by using thin-layer chromatography (TLC) on silica gel-coated plastic sheets (Merck silica gel F_{254})

(25) (a) For a review, see: Sannigrahi M. *Tetrahedron* **1999**, *55*, 9007. (b) Pohmakotr, M.; Bunlaksananusorn, T.; Tuchinda, P. *Tetrahedron Lett.* **2000**, *41*, 377.

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with the solvent (mixture) mentioned before unless noted otherwise. Melting points are uncorrected. Dry THF and Et_2O were distilled from sodium benzophenone ketyl prior to use. Dry DMF, CH_2Cl_2, and MeCN were distilled from CaH_2 and stored over MS 4 Å under a dry nitrogen atmosphere. Triethylamine was dried and distilled from KOH pellets. All commercially available reagents were used as received, unless indicated otherwise.

5-But-3-enyl-2,2,6-trimethyl[1,3]dioxin-4-one (8). To a solution of 2-acetylhex-5-enoic acid *tert*-butyl ester[9] (2.38 g, 11.2 mmol) and Ac_2O (3.8 mL, 40 mmol) in acetone (1.8 mL) was added, dropwise at −10 °C, concentrated H_2SO_4 (0.7 mL). The solution was allowed to warm to room temperature over 16 h. The reaction mixture was poured into ice−water (150 mL) and subsequently stirred for 1 h. The aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 1:6) afforded **8** (1.25 g, 57%) as a colorless oil. $R_f = 0.25$. ^{1}H NMR: 5.80 (ddt, J = 17.0, 10.2, 6.8, 1H), 5.06−4.96 (m, 2H), 2.38−2.35 (m, 2H), 2.26−2.20 (m, 2H), 1.98 (s, 3H), 1.64 (s, 6H). IR: 1718, 1644.

5-Allyl-2,2,6-trimethyl-[1,3]dioxin-4-one (11). To a solution of 2-acetylpent-4-enoic acid *tert*-butyl ester[10] (1.0 g, 5.0 mmol) and Ac_2O (1.7 mL, 18 mmol) in acetone (0.8 mL) was added, dropwise at −10 °C, concentrated H_2SO_4 (0.3 mL). The solution was allowed to warm to room temperature over 16 h. The reaction mixture was poured into ice−water (50 mL) and subsequently stirred for 1 h. The aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 1:5) afforded **11** (575 mg, 63%) as a colorless oil. $R_f = 0.28$. ^{1}H NMR: 5.82 (ddt, J = 17.1, 10.1, 6.1 Hz, 1H), 5.07−5.00 (m, 2H), 3.02 (d, J = 6.1 Hz, 2H), 1.97 (s, 3H), 1.66 (s, 6H). ^{13}C NMR: 164.2, 161.8, 134.9, 114.9, 104.8, 102.8, 28.8, 24.9, 17.2. IR: 1710, 1644.

(2,2,6-Trimethyl-4-oxo-4*H*-[1,3]dioxin-5-yl)acetaldehyde (12). To a solution of **11** (10.0 g, 55 mmol) in THF/water (600 mL, 1:1 v/v) were added, at 0 °C, osmium tetraoxide (10 mL, 1 wt % solution in water, 0.4 mmol) and $NaIO_4$ (28 g, 131 mmol). The resulting mixture was allowed to warm to room temperature and stirred for 7 h. Then, most of the THF was evaporated, and the remaining mixture was diluted with water (500 mL) and extracted with EtOAc. The combined organic layers were washed with 1 N $NaHSO_3$, water, 2 N $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 1:1) afforded **12** (7.57 g, 75%) as a pale yellow semisolid. $R_f = 0.27$. ^{1}H NMR: 9.69 (s, 1H), 3.43 (s, 2H), 1.94 (s, 3H), 1.72 (s, 6H). ^{13}C NMR (in C_6D_6): 197.9, 165.72, 161.9, 106.0, 99.2, 40.6, 25.4, 17.7. IR: 1722, 1650. HRMS (FAB) calculated for $C_9H_{13}O_4$ (MH^+) 185.0814, found 185.0809.

5-(2-Hydroxy-but-3-enyl)-2,2,6-trimethyl-[1,3]dioxin-4-one (13). To a solution of aldehyde **12** (265 mg, 1.44 mmol) in THF (1 mL) was added at −78 °C vinylmagnesium bromide (1.5 mL, 1.0 M solution in THF, 1.5 mmol), and the resulting solution was stirred at −78 °C for 15 min. Saturated aqueous NH_4Cl was added, and the resulting mixture was allowed to warm to room temperature and diluted with EtOAc. The layers were separated, and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to yield an inseparable mixture of the desired alcohol **13** and starting material **12** (60:40, 323 mg). The crude product was used in the next reaction without further purification. ^{1}H NMR: 5.93−5.83 (ddd, J = 17.1, 10.4, 5.8 Hz, 1H), 5.27 (dt, J = 17.1, 1.5 Hz, 1H), 5.12 (dt, J = 10.4, 1.4 Hz, 1H), 4.30 (m, 1H), 2.57 (dd, J = 14.5, 4.9 Hz, 1H), 2.47 (dd, J = 14.5, 7.4 Hz, 1H), 2.38 (br, 1H, O*H*), 2.01 (s, 3H), 1.66 (s, 3H), 1.65 (s, 3H).

Representative Procedure for the Nozaki−Hiyama−Kishi Coupling Reactions with Aldehyde 12. To a solution of aldehyde **12** (325 mg, 1.76 mmol) in DMF (5 mL) at 0 °C were added $CrCl_2$ (1.08 g, 8.8 mmol), $NiCl_2$ (2 mg, 0.02 mmol), and cyclohexenyl triflate[12] (1.2 g, 5.2 mmol). The mixture was allowed to warm to room temperature and stirred at room temperature for 20 h. Saturated aqueous NH_4Cl was added, and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 1:2) afforded **5-(2-cyclohex-1-enyl-2-hydroxyethyl)-2,2,6-trimethyl-[1,3]dioxin-4-one 17a** (402 mg, 86%) as a colorless oil. $R_f = 0.25$. ^{1}H NMR: 5.62 (br, 1H), 4.08−4.05 (m, 1H), 2.51 (dd, J = 14.4, 5.1 Hz, 1H), 2.43 (dd, J = 14.4, 7.7 Hz, 1H), 2.38 (br, 1H), 2.08−1.89 (m, 4H), 1.96 (s, 3H), 1.63−1.44 (m, 4H), 1.61 (s, 6H). ^{13}C NMR: 164.5, 163.0, 139.4, 122.5, 104.7, 102.4, 75.4, 31.2, 24.9, 24.7, 24.5, 23.6, 22.3, 17.5. IR: 3600−3300, 1705, 1644. HRMS (FAB) calculated for $C_{15}H_{23}O_4$ (MH^+) 267.1596, found 267.1598.

5-(2-Cyclopent-1-enyl-2-hydroxyethyl)-2,2,6-trimethyl-[1,3]dioxin-4-one (17b). The reaction of aldehyde **12** (221 mg, 1.2 mmol) with cyclopentenyl triflate[12] (510 mg, 2.4 mmol) at room temperature for 20 h afforded **17b** (193 mg, 64%) as a colorless oil after purification (EtOAc:PE = 1:4). $R_f = 0.13$. ^{1}H NMR: 5.62 (br, 1H), 4.40 (br, 1H), 2.61 (dd, J = 14.5, 4.4 Hz, 1H), 2.49 (dd, J = 14.5, 8.2 Hz, 1H), 2.34−2.29 (m, 5H), 2.00 (s, 3H), 2.00−1.75 (m, 2H), 1.65 (s, 6H). IR: 3600−3300, 1714, 1644. HRMS (EI) calculated for $C_{14}H_{20}O_4$ 252.1362, found 252.1362.

5-(2-Hydroxy-3-methylbut-3-enyl)-2,2,6-trimethyl-[1,3]-dioxin-4-one (17c). The reaction of aldehyde **12** (431 mg, 2.3 mmol) with 2-bromopropene (420 μL, 4.7 mmol) at room temperature for 3 h afforded the product **17c** (527 mg) as a yellow oil. The crude product was used in the next reaction without further purification. ^{1}H NMR: 5.17 (br, 1H), 4.93 (br, 1H), 4.15 (dd, J = 7.8, 4.4 Hz, 1H), 2.81−2.79 (br, 1H), 2.54 (dd, J = 14.6, 4.4 Hz, 1H), 2.41 (dd, J = 14.6, 7.7 Hz, 1H), 1.97 (s, 3H), 1.73 (s, 3H), 1.62 (s, 6H).

5-(2-Hydroxy-(*E*)-pent-3-enyl)-2,2,6-trimethyl-[1,3]dioxin-4-one (17d). The reaction of aldehyde **12** (307 mg, 1.7 mmol) with (*E*)-1-bromo-1-propene (400 μL, 4.7 mmol) at room temperature for 20 h afforded an inseparable mixture of starting material **12** and desired alcohol **17d** (1:9, 254 mg) as a yellow oil. The crude product was used in the next reaction without further purification. ^{1}H NMR: 5.63 (dq, J = 15.0, 6.4 Hz, 1H), 5.28 (ddq, J = 15.2, 5.5, 1.5 Hz, 1H), 4.12−4.07 (m, 1H), 2.53 (dd, J = 14.4, 5.2 Hz, 1H), 2.46 (dd, J = 14.4, 6.9 Hz, 1H), 2.00 (s, 3H), 1.69 (dd, J = 6.4, 1.5 Hz, 3H), 1.65 (s, 3H), 1.63 (s, 3H).

3-(2,2,6-Trimethyl-4-oxo-4*H*-[1,3]dioxin-5-ylmethyl)-4,5,6,7-tetrahydro-3*H*-isobenzofuran-1-one (28). The reaction of aldehyde **12** (300 mg, 1.6 mmol) with vinyl triflate **27**[17] (950 mg, 3.3 mmol) at 50 °C for 7 h afforded **28** (375 mg, 79%) as a white powder after purification (EtOAc:PE = 1:1). R_f = 0.28. ^{1}H NMR: 4.99 (br, 1H), 2.89 (dd, J = 14.8, 3.8 Hz, 1H), 2.58 (dd, J = 14.8, 6.4 Hz, 1H), 2.58−2.52 (m, 1H), 2.26−2.04 (m, 3H), 2.04 (s, 3H), 1.72−1.64 (m. 4H), 1.66 (s, 3H), 1.57 (s, 3H). ^{13}C NMR: 172.9, 167.1, 163.7, 161.7, 126.8, 104.8, 98.6, 81.7, 27.9, 25.7, 23.4, 22.9, 21.2, 21.2, 19.8, 17.9. IR: 1748, 1706, 1639. HRMS (FAB) calculated for $C_{16}H_{21}O_5$ (MH^+) 293.1389, found 293.1395.

2-[1-Hydroxy-2-(2,2,6-trimethyl-4-oxo-4*H*-[1,3]dioxin-5-yl)ethyl)cyclopent-1-enecarboxylic Acid Methyl Ester (31). The reaction of aldehyde **12** (133 mg, 0.72 mmol) with vinyl triflate **29**[18] (396 mg, 1.44 mmol) at 50 °C for 18 h afforded **30** (164 mg, 73%) as a colorless oil after purification (EtOAc:PE = 1:2). $R_f = 0.29$. ^{1}H NMR: 4.84−4.77 (br, 1H), 4.34−4.32 (br, 1H), 3.74 (s, 3H), 2.80−2.71 (m, 2H), 2.70−2.55 (m, 4H), 2.10 (s, 3H), 1.89−1.81 (m, 2H), 1.67 (s, 3H), 1.66 (s, 3H).

Representative Procedure for the Preparation of the MOM Protected Products. To a solution of alcohol **17a** (215 mg, 0.81 mmol) and DIPEA (0.65 mL, 3.7 mmol) in CH_2Cl_2 (12 mL) at 0 °C was added MOMCl (170 μL, 2.3 mmol). The mixture was stirred at 0 °C for 1 h and subsequently at room temperature for 18 h. Saturated aqueous NH_4Cl was added. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 1:3) afforded **5-(2-Cyclohex-1-enyl-2-methoxymethoxyethyl)-**

2,2,6-trimethyl-[1,3]dioxin-4-one 18a (213 mg, 85%) as a colorless oil. R_f = 0.27. ^{1}H NMR: 5.62 (br, 1H), 4.56 (d, J = 6.5 Hz, 1H), 4.45 (d, J = 6.5 Hz, 1H), 4.05 (t, J = 7.0 Hz, 1H), 3.31 (s, 3H), 2.56 (dd, J = 14.2, 6.8 Hz, 1H), 2.49 (dd, J = 14.2, 7.2 Hz, 1H), 2.00−1.89 (m, 4H), 2.00 (s, 3H), 1.63−1.45 (m, 4H), 1.63 (s, 3H), 1.61 (s, 3H). ^{13}C NMR: 164.5, 161.9, 136.2, 126.4, 104.6, 102.2, 93.6, 79.8, 55.4, 29.6, 25.0, 25.0, 24.8, 22.8, 22.5, 22.4, 17.8. IR: 1710, 1644. HRMS (EI) calculated for $C_{17}H_{27}O_5$ 311.1858, found 311.1858.

5-(2-Methoxymethoxybut-3-enyl)-2,2,6-trimethyl-[1,3]-dioxin-4-one (14). The mixture of aldehyde **12** and alcohol **13** (2:3, 323 mg) afforded the MOM protected product **14** (157 mg, 43% from aldehyde **12**) as a colorless oil and recovered aldehyde **12** (58 mg, 22%) after purification (EtOAc:PE = 1:2). R_f = 0.34. ^{1}H NMR: 5.69 (ddd, J = 17.6, 10.3, 7.6 Hz, 1H), 5.23−5.15 (m, 2H), 4.62 (d, J = 6.6 Hz, 1H), 4.52 (d, J = 6.6 Hz, 1H), 4.16 (q, J = 6.7 Hz, 1H), 3.31 (s, 3H), 2.51 (d, J = 6.7 Hz, 2H), 1.99 (s, 3H), 1.62 (s, 3H), 1.61 (s, 3H). ^{13}C NMR: 165.0, 162.0, 137.8, 117.5, 104.7, 101.4, 94.0, 76.6, 55.3, 31.3, 25.1, 24.8, 17.8. IR: 1716, 1645. HRMS (EI) calculated for $C_{13}H_{20}O_5$ 256.1311, found 256.1304.

5-(2-Cyclopent-1-enyl-2-methoxymethoxyethyl)-2,2,6-trimethyl-[1,3]dioxin-4-one (18b). Alcohol **17b** (131 mg, 0.52 mmol) afforded the MOM protected product **18b** (102 mg, 66%) as a colorless oil after purification (EtOAc:PE = 1:3). R_f = 0.25. ^{1}H NMR: 5.59 (br, 1H), 4.54 (d, J = 6.5 Hz, 1H), 4.46 (d, J = 6.5 Hz, 1H), 4.37 (t, J = 6,9 Hz, 1H), 3.29 (s, 3H), 2.55 (dd, J = 14.2, 7.0 Hz, 1H), 2.49 (dd, J = 14.2, 7.0 Hz, 1H), 2.32−2.20 (m, 4H), 1.98 (s, 3H), 1.86−1.79 (m, 2H), 1.61 (s, 3H), 1.59 (s, 3H). ^{13}C NMR: 164.7, 161.9, 143.3, 129.0, 104.6, 102.0, 94.0, 74.3, 55.4, 32.0, 30.3, 30.0, 25.1, 24.7, 23.2, 17.7. IR: 1706, 1632. HRMS (EI) calculated for $C_{16}H_{24}O_5$ 296.1624, found 296.1618.

5-(2-Methoxymethoxy-3-methylbut-3-enyl)-2,2,6-trimethyl-[1,3]dioxin-4-one (18c). Alcohol **17c** (527 mg, 2.3 mmol) afforded the MOM protected product **18c** (437 mg, 69% from aldehyde **12**) as a colorless oil after purification (EtOAc:PE = 1:4). R_f = 0.20. ^{1}H NMR: 4.93 (br, 1H), 4.91 (br, 1H), 4.55 (d, J = 6.5 Hz, 1H), 4.48 (d, J = 6.5 Hz, 1H), 4.17−4.13 (m, 1H), 3.31 (s, 3H), 2.57 (dd, J = 14.3, 6.1 Hz, 1H), 2.49 (dd, J = 14.3, 7.1 Hz, 1H), 2.01 (s, 3H), 1.72 (s, 3H), 1.64 (s, 3H), 1.62 (s, 3H). ^{13}C NMR: 164.8, 161.9, 143.9, 114.0, 104.6, 101.8, 93.9, 79.1, 55.4, 29.9, 25.1, 24.8, 17.7, 16.8. IR: 1722, 1645. HRMS (FAB) calculated for $C_{14}H_{23}O_5$ (MH^+) 271.1545, found 271.1543.

5-(2-Methoxymethoxy-(*E*)-pent-3-enyl)-2,2,6-trimethyl-[1,3]dioxin-4-one (18d). The mixture of aldehyde **12** and alcohol **17d** (1:9, 254 mg) afforded the MOM protected product **18d** (129 mg, 29% from aldehyde **12**) as a colorless oil after purification (EtOAc:PE = 1:4). R_f = 0.18.^{1}H NMR: 5.65 (ddq, J = 15.2, 6.5, 0.5 Hz, 1H), 5.30 (ddq, J = 15.2, 8.4, 1.6 Hz, 1H), 4.66 (d, J = 6.6 Hz, 1H), 4.50 (d, J = 6.6 Hz, 1H), 4.11 (semiq, 1H), 3.32 (s, 3H), 2.53 (dd, J = 14.1, 7.0 Hz, 1H), 2.48 (dd, J = 14.1, 6.9 Hz, 1H), 2.00 (s, 3H), 1.68 (dd, J = 6.5, 1.6 Hz, 3H), 1.64 (s, 3H), 1.62 (s, 3H). ^{13}C NMR: 164.7, 161.9, 130.7, 129.5, 104.6, 101.7, 93.4, 76.1, 55.2, 31.4, 25.0, 24.7, 17.7, 17.5. IR: 1722, 1647. HRMS (FAB) calculated for $C_{14}H_{23}O_5$ (MH^+) 271.1545, found 271.1550.

2-[1-Methoxymethoxy-2-(2,2,6-trimethyl-4-oxo-4*H*-[1,3]-dioxin-5-yl)ethyl]cyclopent-1-enecarboxylic Acid Methyl Ester (31). Alcohol **30** (117 mg, 0.38 mmol) afforded the MOM protected product **31** (73 mg, 55%) as a colorless oil after purification (EtOAc:PE = 1:1). R_f = 0.38. ^{1}H NMR: 5.41 (t, J = 14.2 Hz, 1H, H-9), 4.54 (s, 2H, $CH_3OC\mathit{H}_2O$), 3.71 (s, 3H, C(O)OCH_3), 3.34 (s, 3H, CH_3OCH_2O), 2.78−2.45 (m, 6H), 2.07 (s, 3H, H-7), 1.90−1.73 (m, 2H), 1.63 (s, 3H, CH_3), 1.60 (s, 3H, CH_3). ^{13}C NMR: 165.9 (*C*(O)OCH$_3$), 165.3 (C-4), 161.9 (C-6), 157.4 (C-10), 130.9 (C-14), 104.7 (C-2), 101.0 (C-5), 95.4 (CH_3OCH_2O), 72.2 (C-9), 55.8 (CH_3OCH_2O), 51.2 (C(O)O*C*H$_3$), 34.0, 33.1, 29.4, 25.4 (*C*H$_3$), 24.6 (*C*H$_3$), 21.6, 17.7 (C-7). IR: 1712, 1642. HRMS (FAB) calculated for $C_{18}H_{27}O_7$ (MH^+) 355.1757, found 355.1765.

Representative Procedure for the Oxidation of the Alcohols 17a and 17b. To a solution of oxalyl chloride (113 μL, 1.28 mmol) in CH_2Cl_2 (4 mL) was added dropwise, at −60 °C → -50 °C, DMSO (166 μL, 2.34 mmol), then after 5 min a solution of alcohol **17a** (312 mg, 1.17 mmol) in CH_2Cl_2 (2 mL), and finally, after 30 min triethylamine (0.74 mL, 5.3 mmol). The mixture was stirred for 5 min and allowed to warm to room temperature, and stirring was continued for 15 min. Water was added, and the resulting mixture was stirred for 15 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with saturated aqueous NH_4Cl, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 1:4) afforded **5-(2-Cyclohex-1-enyl-2-oxoethyl)-2,2,6-trimethyl-[1,3]dioxin-4-one 19a** (294 mg, 95%) as a colorless oil. R_f = 0.19. ^{1}H NMR: 7.05 (br, 1H), 3.63 (s, 2H), 2.36−2.21 (m, 4H), 1.88 (s, 3H), 1.73 (s, 6H), 1.65−1.52 (m, 4H). ^{13}C NMR: 197.0, 165.4, 162.2, 140.8, 138.6, 105.3, 100.3, 33.3, 26.1, 24.9, 23.1, 21.8, 21.4, 17.4. IR: 1709, 1651. HRMS (EI) calculated for $C_{15}H_{20}O_4$ 264.1362, found 264.1357.

5-(2-Cyclopent-1-enyl-2-oxoethyl)-2,2,6-trimethyl-[1,3]-dioxin-4-one (19b). The oxidation of alcohol **17b** (161 mg, 0.64 mmol) afforded ketone **19b** (124 mg, 77%) as a colorless oil after purification (EtOAc:PE = 1:3). R_f = 0.30. ^{1}H NMR: 6.89 (br, 1H), 3.69 (s, 2H), 2.58−2.24 (m, 4H), 1.94−1.91 (m, 2H), 1.93 (s, 3H), 1.73 (s, 6H). ^{13}C NMR: 194.5, 165.5, 162.1, 144.6, 144.4, 105.2, 99.9, 34.9, 33.9, 30.5, 24.7, 22.5, 17.6. IR: 1718, 1669.

Representative Procedure for the Preparation of the Acetal-Protected Products 20a and 20b. To a solution of ketone **19a** (165 mg, 0.62 mmol) in CH_2Cl_2 (2 mL) at −78 °C were added dropwise $(TMSOCH_2)_2$ (400 μL, 1.63 mmol) and TMSOTf (44 μL, 0.24 mmol). The mixture was allowed to warm to 0 °C over 1 h and kept at 0 °C for 30 h. Saturated aqueous $NaHCO_3$ was added, and the resulting mixture was stirred for 15 min. The layers were separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 1:4) afforded **5-(2-Cyclohex-1-enyl-[1,3]dioxolan-2-ylmethyl)-2,2,6-trimethyl-[1,3]dioxin-4-one 20a** (127 mg, 66%) as a colorless oil. R_f = 0.24. ^{1}H NMR: 5.77 (br, 1H), 3.84−3.82 (m, 2H), 3.76−3.72 (m, 2H), 2.73 (s, 2H), 2.05−2.03 (m, 2H), 1.98 (s, 3H), 1.96−1.87 (m, 2H), 1.61 (s, 6H), 1.58−1.56 (m, 2H), 1.50−1.47 (m, 2H). ^{13}C NMR: 165.5, 162.2, 136.5, 123.7, 111.0, 104.3, 100.9, 64.0, 31.6, 24.8, 24.7, 23.9, 22.5, 21.8, 18.2. IR: 1721, 1645. HRMS (FAB) calculated for $C_{17}H_{25}O_5$ (MH^+) 309.1702, found 309.1714.

5-(2-Cyclopent-1-enyl-[1,3]dioxolan-2-ylmethyl)-2,2,6-trimethyl-[1,3]dioxin-4-one (20b). Ketone **19b** (79 mg, 0.32 mmol) afforded acetal **20b** (61 mg, 66%) as a colorless oil after purification (EtOAc:PE = 1:6). R_f = 0.13. ^{1}H NMR: 5.71−5.69 (m, 1H), 3.93−3.90 (m, 2H), 3.87−3.82 (m, 2H), 2.82 (s, 2H), 2.43−2.39 (m, 2H), 2.33−2.27 (m, 2H), 2.01 (s, 3H), 1.93−1.85 (m, 2H), 1.55 (s, 6H). ^{13}C NMR: 165.6, 162.2, 144.0, 127.9, 109.3, 104.2, 100.6, 64.2, 32.2, 31.6, 31.4, 24.7, 23.6, 18.1. IR: 1722, 1644.

Representative Procedure for the Intramolecular [2 + 2] Cycloadditions. The photoreaction was carried out in a Pyrex glass vessel with a Rayonet RPR 3000 Å at room temperature. A solution of acetal **20a** (127 mg, 0.41 mmol) in acetonitrile/acetone (20 mL, 9:1 v/v) was degassed by bubbling argon through for 30 min. The solution was kept under argon and irradiated for 90 min. The reaction was followed by monitoring the UV absorption of the starting material on TLC. The solvent was removed in vacuo. Purification by chromatography (EtOAc:PE = 1:2) afforded adduct **23** (121 mg, 95%) as a colorless oil. R_f = 0.40. ^{1}H NMR: 4.05−3.74 (m, 4H), 3.14 (d, J = 14.8 Hz, 1H), 2.70 (dd, J = 9.1, 6.7 Hz, 1H), 2.58 (d, J = 14.1 Hz, 1H), 1.98−1.89 (m, 1H), 1.73−1.39 (m, 5H), 1.58 (s, 3H), 1.55 (s, 3H), 1.51 (s, 3H), 1.26−1.13 (m, 2H). ^{13}C NMR: 169.2, 108.1, 104.5, 77.4, 65.0, 64.4, 58.1, 41.7, 41.1, 36.7, 29.5, 29.2, 24.1, 21.1, 20.9, 20.3, 18.6. IR: 1730. HRMS (FAB) calculated for $C_{17}H_{25}O_5$ (MH^+) 309.1702, found 309.1695.

4,4,6-Trimethyl-3,5-dioxatricyclo[5.2.1.0^{1,6}]decan-2-one (9). Irradiation of a solution of **8** (50 mg, 0.26 mmol) in acetonitrile/acetone (15 mL, 9:1 v/v) for 3.5 h afforded the

unstable cycloadduct **9** (50 mg, 100% crude yield) as a yellow oil. The crude product was used immediately in the next reaction without further purification. ^{1}H NMR (C_6D_6): 2.56−2.53 (m, 1H), 2.11−2.09 (m, 1H), 1.95−1.89 (m, 1H), 1.46−1.37 (m, 1H), 1.41 (s, 3H), 1.32−1.15 (m, 2H), 1.30 (s, 3H), 1.03 (d, J = 6.5 Hz, 1H), 0.88 (s, 3H). ^{13}C NMR (C_6D_6): 169.8, 109.8, 83.9, 51.0, 46.2, 42.8, 30.9, 30.7, 25.5, 23.5.

8-Methoxymethoxy-4,4,6-trimethyl-3,5-dioxatricyclo-[5.2.1.0^{1,6}]decan-2-one (15). Irradiation of a solution of **14** (157 mg, 0.61 mmol) in acetonitrile/acetone (20 mL, 9:1 v/v) for 3 h afforded the unstable cycloadduct **15** (159 mg, 100% crude yield) as yellow oil. The crude product was used immediately in the next reaction without further purification. ^{1}H NMR: 4.40 (d, J = 6.9 Hz, 1H), 4.37 (d, J = 6.9 Hz, 1H), 4.31 (s, 2H), 3.92 (dd, J = 6.6, 1.6 Hz, 1H), 3.83−3.81 (m, 1H), 3.07 (s, 3H), 3.04 (s, 3H), 2.68−2.66 (m, 1H), 2.54−2.44 (m, 4H), 2.07 (dd, J = 12.3, 1.7 Hz, 1H), 1.98 (d, J = 6.6 Hz, 1H), 1.93 (ddd, J = 12.3, 6.8, 2.9 Hz, 1H), 1.69−1.65 (m, 1H), 1.47 (s, 3H), 1.41 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.26 (s, 3H), 0.87 (d, J = 6.9 Hz, 1H), 0.77 (s, 3H).

Cycloadduct 21. Irradiation of a solution of **18a** (145 mg, 0.47 mmol) in acetonitrile/acetone (25 mL, 9:1 v/v) for 30 min afforded a 50:50 mixture of diastereomers **21a** and **21b** (120 mg, 83%) as colorless oil after purification (EtOAc:PE = 1:2). R_f = 0.29 and R_f = 0.26. ^{1}H NMR: 4.64 (d, J = 6.6 Hz, 1H), 4.59 (d, J = 6.6 Hz, 1H), 4.57 (d, J = 4.4 Hz, 1H), 4.55 (d, J = 4.4 Hz, 1H), 4.15 (t, J = 6.4 Hz, 1H), 4.04 (dd, J = 9.7, 6.6 Hz, 1H), 3.36 (s, 3H), 3.35 (s, 3H), 3.00 (dd, J = 13.4, 9.7 Hz, 1H), 2.79 (dd, J = 9.7, 4.5 Hz, 1H), 2.74 (dd, J = 13.0, 6.5 Hz, 1H), 2.53 (dd, J = 13.0, 6.4 Hz, 1H), 2.16 (t, J = 7.4 Hz, 1H), 2.13 (dd, J = 13.4, 6.6 Hz, 1H), 2.00−1.00 (m, 8H), 1.59 (s, 6H), 1.56 (s, 3H), 1.52 (s, 6H) 1.45 (s, 3H). ^{13}C NMR: 169.8, 169.1, 104.8, 103.9, 78.6, 77.0, 76.0, 55.5, 52.3, 52.2, 49.8, 43.7, 42.5, 31.2, 29.5, 29.4, 29.1, 29.1, 28.4, 27.9, 24.7, 22.9, 21.6, 21.5, 20.9, 20.9, 20.8, 20.6, 18.4. IR: 1714. HRMS (EI) calculated for $C_{17}H_{26}O_5$ 310.1780, found 310.1776.

Cycloadduct 22. Irradiation of a solution of **18b** (92 mg, 0.31 mmol) in acetonitrile/acetone (20 mL, 9:1 v/v) for 30 min afforded a 43:57 mixture of diastereomers **22a** and **22b** (89 mg, 97%) as a colorless oil after purification (EtOAc:PE = 1:2). R_f = 0.27 and R_f = 0.22. ^{1}H NMR: 4.65 (d, J = 6.8 Hz, 1H), 4.60 (d, J = 6.8 Hz, 1H), 4.59 (d, J = 6.6 Hz, 1H), 4.55 (d, J = 6.6 Hz, 1H), 4.36 (dd, J = 5.9, 5.9 Hz, 1H), 4.31 (dd, J = 9.9, 5.9 Hz, 1H), 3.36 (s, 3H), 3.32 (s, 3H), 2.95 (dd, J = 13.6, 9.9 Hz, 1H), 2.88 (d, J = 9.0 Hz, 1H), 2.80 (dd, J = 13.6, 5.1 Hz, 1H), 2.58 (dd, J = 13.6, 6.3 Hz, 1H), 2.35 (d, J = 9,0 Hz, 1H), 2.25 (dd, J = 13.6, 5.9 Hz, 1H), 2.12−2.05 (m, 1H), 2.10 (dd, J = 13.9, 6.8 Hz, 1H), 1.94 (dd, J = 13.8, 5.7 Hz, 1H), 1.83−1.66 (m, 3H), 1.82−1.36 (m, 4H), 1.60 (s, 3H), 1.55 (s, 3H), 1.52 (s, 3H) 1.51 (s, 3H), 1.50−1.39 (m, 2H), 1.46 (s, 3H), 1.44 (s, 3H). ^{13}C NMR: 170.1, 104.3, 103.9, 96.0, 95.3, 76.0, 74.5, 74.2, 62.2, 61.7, 55.6, 55.4, 54.2, 48.0, 42.6, 41.4, 31.6, 29.3, 29.2, 28.9, 28.6, 27.4, 26.4, 25.8, 25.3, 25.1, 24.9. IR: 1714.

Cycloadduct 24. Irradiation of a solution of acetal **20b** (64 mg, 0.22 mmol) in acetonitrile/acetone (15 mL, 9:1 v/v) for 75 min afforded **24** (64 mg, 100% crude yield) as a white powder. The crude product was used immediately in the next reaction without further purification. An analytically pure sample was obtained after chromatography (EtOAc:PE = 1:3) to afford **24** as a white powder. R_f = 0.3. mp 126−127 °C. ^{1}H NMR: 4.03−3.82 (m, 4H), 3.13 (d, J = 14.0 Hz, 1H), 2.76 (br d, J = 9.0 Hz, 1H), 2.62 (d, J = 14.0 Hz, 1H), 2.13 (dd, J = 13.4, 6.6 Hz, 1H), 1.92 (dd, J = 14.2, 5.8 Hz, 1H), 1.73−1.64 (m, 3H), 1.60 (s, 3H), 1.53 (s, 3H), 1.48 (s, 3H), 1.42−1.36 (m, 1H). ^{13}C NMR: 169.9, 106.8, 104.0, 74.8, 67.4, 65.0, 64.6, 49.0, 39.0, 37.6, 29.2, 28.6, 27.7, 25.9, 25.6, 25.3. IR: 1729. HRMS (FAB) calculated for $C_{16}H_{23}O_5$ (MH^+) 295.1545, found 295.1555.

3-Methoxymethoxy-4,6,8,8-tetramethyl-7,9-dioxatricyclo[4.4.0.0^{1,4}]decan-10-one (25). Irradiation of a solution of alkene **18c** (277 mg, 1.03 mmol) in acetonitrile/acetone (50 mL, 9:1 v/v) for 2−3 h afforded **25** (130 mg, 47%) as a colorless oil after purification (EtOAc:PE = 1:3). R_f = 0.24. ^{1}H NMR: 4.58 (d, J = 6.6 Hz, 1H), 4.53 (d, J = 6.6 Hz, 1H), 4.06 (dd, J = 9.8, 6.7 Hz, 1H), 3.32 (s, 3H), 3.07 (dd, J = 13.5, 9.8 Hz, 1H), 2.65 (d, J = 13.2 Hz, 1H), 2.11 (dd, J = 13.6, 6.8 Hz, 1H), 1.93 (d, J = 13.2 Hz, 1H), 1.56 (s, 6H), 1.53 (s, 3H), 1.26 (s, 3H). ^{13}C NMR: 168.9, 104.9, 95.7, 77.1, 74.9, 55.4, 50.1, 42.4, 39.6, 29.8, 29.3, 27.6, 23.0, 21.3. IR: 1729. HRMS (FAB) calculated for $C_{14}H_{23}O_5$ (MH^+) 271.1545, found 271.1539.

3-Methoxymethoxy-5,6,8,8-tetramethyl-7,9-dioxatricyclo[4.4.0.0^{1,4}]decan-10-one (26). Irradiation of a solution of alkene **18d** (111 mg, 0.41 mmol) in acetonitrile/acetone (20 mL, 9:1 v/v) for 6.5 h afforded a mixture of straight adducts (70:20:10) **26** (40 mg, 36%) as a colorless oil after purification (EtOAc:PE = 1:7). R_f = 0.12. **Main adduct:** ^{1}H NMR (C_6D_6): 4.49 (ddd, J = 9.6, 6.7, 4.3 Hz, 1H), 4.36 (d, J = 6.5 Hz, 1H), 4.34 (d, J = 6.5 Hz, 1H), 3.28 (ddd, J = 13.1, 9.6, 2.5 Hz, 1H), 3.13 (s, 3H), 2.77 (dq, J = 7.2, 4.7 Hz, 1H), 2.62 (ddd, J = 6.8, 4.7, 2.5 Hz, 1H), 2.23 (dd, J = 13.2, 6.9 Hz, 1H), 1.42 (s, 3H), 1.22 (s, 3H), 1.13 (s, 3H), 1.07 (d, J = 7.2, 3H). IR: 1731. HRMS (FAB) calculated for $C_{14}H_{23}O_5$ (MH^+) 271.1545, found 271.1552.

Cycloadduct 3. Irradiation of a solution of alkene **28** (100 mg, 0.34 mmol) in acetonitrile/acetone (20 mL, 9:1 v/v) for 2 h afforded **3** (95 mg, 95% crude yield), which was used in the next reaction without further purification. X-ray crystal structure determination was allowed after recrystallization from CH_2Cl_2/pentane. Colorless crystals. mp 177−178 °C. ^{1}H NMR: 4.54 (d, J = 4.2 Hz), 2.39 (dt, J = 13.3, 4.7 Hz, 1H), 2.33 (dd, J = 12.8, 4.2 Hz, 1H), 2.23−2.20 (m, 1H), 1.98 (d, J = 12.8 Hz, 1H), 1.89−1.85 (m, 1H), 1.81−1.61 (m, 2H), 1.73 (s, 3H), 1.64 (s, 3H), 1.56−1.40 (m, 2H), 1.40 (s, 3H), 1.05−0.93 (m, 1H). ^{13}C NMR: 174.7, 164.9, 109.9, 83.2, 79.7, 62.1, 60.4, 51.5, 33.7, 31.1, 29.2, 21.8, 21.7, 21.4, 20.4, 19.4.

Cycloadduct 4. Irradiation of a solution of **31** (61 mg, 0.17 mmol) in acetonitrile/acetone (11.1 mL, 9:1 v/v) for 60 min afforded a 40:60 mixture of diastereomers **4a** and **4b** (47 mg, 78%) as colorless oil after purification (EtOAc:PE = 1:1). Repeated chromatography led to pure isomers. **4a:** X-ray crystal structure determination was allowed after recrystallization from CH_2Cl_2/pentane. Colorless crystals. R_f = 0.41. mp 62−64 °C. ^{1}H NMR: 4.55 (d, J = 0.6.6 Hz, 1H), 4.50−4.46 (m. 2H), 3.62 (s, 3H), 3.32 (s, 3H), 2.91 (dd, J = 13.7, 9.9 Hz, 1H), 2.63−2.56 (m, 1H), 2.29 (dd, J = 13.7, 4,5 Hz, 1H), 2.02−2.02 (m, 1H), 1.92 (s, 3H), 1.87−1.76 (m, 3H), 1.66−1.56 (m, 1H), 1.55 (s, 3H), 1.50 (s, 3H). ^{13}C NMR: 174.2, 170.2, 104.3, 95.6, 77.9, 70.6, 65.0, 60.8, 55.4, 51.0, 40.5, 33.9, 32.8, 29.6, 29.1, 28.6, 24.2, 23.4. IR: 1724. **4b:** colorless oil. R_f = 0.34. ^{1}H NMR: 4.72 (t, J = 6.6 Hz, 1H), 4.68 (d, J = 6.6 Hz, 1H), 4.63 (d, J = 6.6 Hz, 1H), 3.71 (s, 3H), 3.37 (s, 3H), 2.79 (dd, J = 13.2, 6.5 Hz, 1H), 2.58 (dd, J = 13.1, 6.8 Hz, 1H), 2.55−2.52 (m, 1H), 2.11 (dd, J = 12.4, 5.5 Hz, 1H), 1.77−1.44 (m, 4H), 1.60 (s, 3H), 1.55 (s, 3H), 1.44 (s, 3H). ^{13}C NMR: 179.7, 173.1, 104.0, 95.4, 76.3, 70.3, 65.0, 62.5, 55.4, 51.5, 40.2, 32.5, 31.4, 29.3, 28.4, 26.9, 23.2, 22.5.

Representative Procedure for the Reduction Reaction. To a solution of $LiAlH_4$ (1 M in THF, 0.9 mL, 0.9 mmol) was added dropwise at room temperature a solution of the crude cycloadduct **9** (50 mg) in THF (0.5 mL). The reaction mixture was stirred for 10 min. Then, the reaction was quenched by addition of EtOAc, and saturated aqueous Na_2SO_4 (10 drops) was added. The resulting mixture was stirred for 1 h. After addition of additional solid Na_2SO_4, the mixture was filtered through Celite and concentrated in vacuo. Purification by chromatography (EtOAc:PE = 3:1) afforded **1-hydroxymethyl-5-methylbicyclo[2.1.1]hexan-5-ol 10** (17 mg, 47% from **8**) as a white powder. X-ray crystal structure determination was allowed after recrystallization from Et_2O/pentane. Colorless crystals. R_f = 0.25. mp 88−89 °C. ^{1}H NMR: 3.88 (d, J = 11.7 Hz, 1H), 3.75 (d, J = 11.7 Hz, 1H), 2.67−2.65 (m, 1H), 2.55 (br, 1H), 2.35 (br, 1H), 2.26−2.25 (m, 1H), 1.64−1.60 (m, 2H), 1.45−1.52 (m, 2H), 1.15 (s, 3H), 1.04 (d, J = 6.8 Hz, 1H).

1-Hydroxymethyl-3-methoxymethoxy-5-methylbicyclo-[2.1.1]hexan-5-ol (16). The crude cycloadduct **15** (159 mg) afforded a 50:50 mixture of diastereomers **16a** and **16b** (64 mg, 52% from **14**) as a colorless oil after purification (EtOAc). R_f = 0.33. **16a:** ^{1}H NMR (C_6C_6): 4.52 (s, 2H), 4.05 (dd, J = 6.9, 1.6 Hz, 1H), 3.60 (s, 2H), 3.17 (s, 3H), 2.81−2.75 (m, 1H), 2.49−2.48 (m, 1H), 1.73 (ddd, J = 11.8, 6.9, 3.0 Hz, 1H), 1.70 (d, J = 6.6 Hz, 1H), 1.32 (dd, J = 11.8, 2.0 Hz, 1H), 0.92 (s,

3H). ^{13}C NMR (C_6D_6): 96.2, 84.8, 76.0, 63.1, 55.7, 55.3, 51.9, 37.3, 32.6, 18.8. **16b:** ^{1}H NMR (C_6D_6): 4.46 (s, 2H), 3.95 (ddd, J = 8.6, 2.9, 1.7 Hz, 1H), 3.67 (d, J = 11.6 Hz, 1H), 3.53 (d, J = 11.6 Hz, 1H), 3.15 (s, 3H), 2.81−2.75 (m, 1H), 2.45 (dd, J = 3.1, 1.6 Hz, 1H), 1.63 (dd, J = 11.8, 8.6 Hz, 1H), 1.46 (ddd, J = 11.8, 3.9, 3.1 Hz, 1H), 1.46 (s, 3H), 0.77 (d, J = 7.0 Hz, 1H). ^{13}C NMR (C_6D_6): 97.0, 85.2, 78.1, 63.1, 56.2, 55.8, 52.2, 36.6, 35.6, 34.4, 20.2. HRMS (FAB) calculated for $C_{10}H_{19}O_4$ (MH^+) 203.1283, found 203.1284.

1,7a-Bis-hydroxymethyl-8-methyloctahydro-1,3a-methanoindene-3,8-diol (32). The crude cycloadduct **3** (95 mg) afforded the tetraol **32** (43 mg, 52% from **28**) as a white powder after purification (EtOAc:acetone = 1:1). R_f = 0.31. ^{1}H NMR (CD_3OD): 4.38 (dd, J = 11.4, 2.5 Hz, 1H), 3.94 (dd, J = 7.4, 3.1 Hz, 1H), 3.77 (d, J = 11.1 Hz, 1H), 3.38 (d, J = 11.1 Hz, 1H), 3.34 (d, J = 11.4 Hz, 1H), 3.26 (d, J = 11.4 Hz, 1H), 3.03−2.95 (m, 1H), 2.03−1.87 (m, 4H), 1.65−1.61 (m, 1H), 1.55−1.25 (m, 4H), 1.08 (s, 3H). ^{13}C NMR (CD_3OD): 84.5, 73.0, 62.4, 59.1, 58.6, 58.1, 51.9, 37.6, 27.0, 23.0, 22.5, 21.9, 19.3. HRMS calculated for $C_{13}H_{22}O_4Na$ (MNa^+) 265.1416, found 265.1425.

Diol 33. Cycloadduct **23** (96 mg, 0.31 mmol) afforded diol **33** (78 mg, 99%) as a colorless oil without further purification. ^{1}H NMR: 4.01−3.85 (m, 4H), 3.81−3.75 (m, 2H), 2.62 (dd, J = 8.8, 6.4 Hz, 1H), 2.55 (d, J = 13.9 Hz, 1H), 2.40−2.20 (br, 2H), 2.20 (d, J = 13.9 Hz, 1H), 1.81−1.73 (m, 2H), 1.70−1.43 (m, 3H), 1.37−1.26 (m, 1H), 1.27 (s, 3H), 1.14−1.06 (m, 1H). ^{13}C NMR: 109.1, 79.4, 64.5, 64.3, 62.7, 51.6, 45.1, 40.7, 40.5, 24.0, 21.5, 20.8, 19.5, 18.3. HRMS (FAB) calculated for $C_{14}H_{23}O_4$ (MH^+) 255.1596, found 255.1591.

Representative Procedure for the Retro-Aldol Reaction. To a solution of cycloadduct **3** (100 mg, 0.34 mmol) in dioxane (10 mL) at room temperature was added dropwise an aqueous solution of KOH (1.8 mL, 10% *w*/*w*). The mixture was stirred for 150 min. The reaction mixture was cooled to 0 °C, acidified carefully with 2 N HCl to pH 2−3, and extracted with CH_2Cl_2. The combined organic layers were washed brine, dried over $MgSO_4$, and concentrated in vacuo. The remaining mixture was dissolved in methanol (5 mL), cooled to 0 °C, and treated with an excess of diazomethane. After concentration in vacuo, the crude oil was purified by chromatography (EtOAc:PE = 1:1) to afford **6-acetyl-9-oxo-8-oxatricyclo-[5.2.2.0^{1,6}]undecane-10-carboxylic acid methyl ester 34** (71 mg, 78%) as a white powder. R_f = 0.22. mp 144−146 °C (EtOAc/pentane). ^{1}H NMR: 4.75 (br, 1H), 3.69 (s, 3H), 3.29 (dd, J = 10.3, 4.5 Hz, 1H), 2.48 (ddd, J = 14.4, 4.5, 1.0 Hz, 1H), 2.19−2.15 (m, 2H), 2.15 (s, 3H), 1.96 (ddd, J = 6.6, 3.3, 1.3 Hz, 1H), 1.89 (ddd, J = 14.4, 10.3, 2.0 Hz, 1H), 1.74−1.57 (m, 3H), 1.45−1.33 (m, 1H), 1.05 (dq, J = 13.7, 3.6 Hz, 1H). ^{13}C NMR: 205.2, 175.1, 171.8, 78.7, 67.4, 56.8, 52.3, 42.7, 31.6, 25.6, 25.6, 22.3, 21.8, 20.1. IR: 1775, 1732, 1705. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 62.98; H, 6.93.

7-Acetyl-1,4-dioxadispiro[4.0.5.2]tridecane-12-carboxylic Acid Methyl Ester (35). The crude cycloadduct **23** (43 mg, 0.14 mmol) afforded (105 min) a 30:70 mixture of two diastereomers **35a** and **35b** (30 mg, 75%) as a colorless oil after purification (EtOAc:PE = 1:5). Both isomers were obtained pure after repeated chromatography. **35a:** colorless oil. R_f = 0.17. ^{1}H NMR: 3.96−3.75 (m, 4H), 3.56 (s, 3H), 2.60 (dd, J = 9.6, 8.0 Hz, 1H), 2.42 (dd, J = 7.9, 12.6 Hz, 1H), 2.33 (dd, J = 9.6, 12.6 Hz, 1H), 2.21−2.12 (m, 1H), 2.10 (s, 3H), 1.94−1.90 (m, 2H), 1.72 (ddt, J = 13.9, 5.8, 3.5 Hz, 1H), 1.60−1.56 (m, 2H), 1.45−1.38 (m, 1H), 1.32 (qt, J 13.0, 4.0 Hz, 1H), 1.06 (qt, J = 13.2, 3.6 Hz, 1H). ^{13}C NMR: 210.5, 174.8, 108.3, 64.6, 64.3, 55.9, 51.3, 47.3, 40.6, 36.7, 29.9, 29.0, 26.1, 23.9, 21.1. IR: 1723 (br). HRMS (FAB) calculated for $C_{15}H_{23}O_5$ (MH^+) 283.1545, found 283.1540. **35b:** X-ray crystal structure determination was allowed after recrystallization from EtOAc/PE. Colorless crystals. R_f = 0.08. mp 85−87 °C. ^{1}H NMR: 3.94−3.68 (m, 4H), 3.67 (s, 3H), 3.53 (semit, 1H), 2.70 (dd, J = 7.2, 4.1 Hz, 1H), 2.58 (dd, J = 12.6, 9.2 Hz, 1H), 2.19 (s, 3H), 2.14 (dd, J = 12.6, 9.0 Hz, 1H), 2.07−2.02 (m, 1H), 1.64−1.50 (m, 5H), 1.27−1.24 (m, 2H). ^{13}C NMR: 211.1, 174.0, 109.1, 64.7, 64.3, 56.9, 51.6, 51.4, 36.2, 35.2, 30.4, 27.1, 26.4, 23.9, 21.9. IR: 1731, 1711.

7-Acetyl-1,4-dioxa-dispiro[4.0.4.2]dodecane-11-carboxylic Acid Methyl Ester (36). The crude cycloadduct **24** (56 mg, 0.19 mmol) afforded (105 min) a 50:50 mixture of two diastereomers **36a** and **36b** (40 mg, 78% from **20b**) as a colorless oil after purification (Et_2O:PE = 1:3). Both isomers were obtained pure after repeated chromatography. **36a:** white powder. R_f = 0.21. mp 68−71 °C. ^{1}H NMR: 3.94−3.70 (m, 4H), 3.58 (s, 3H), 2.89 (dd, J = 9.3, 7.6 Hz, 1H), 2.45 (dd, J = 12.6, 7.6 Hz, 1H), 2.40 (dd, J = 12.6, 9.3 Hz, 1H), 2.29−2.23 (m, 1H), 2.12 (s, 3H), 2.01 (ddd, J = 13.0, 10.2, 7.9 Hz, 1H), 1.83−1.51 (m, 5H), 1.60 (s, 3H). ^{13}C NMR: 221.1, 175.3, 109.0, 64.8, 64.4, 62.4, 51.6, 51.4, 37.5, 37.3, 32.2, 29.6, 28.6, 21.7. IR: 1728, 1708. HRMS (FAB) calculated for $C_{14}H_{21}O_5$ (MH^+) 269.1389, found 269.1401. **36b:** Colorless oil. R_f = 0.13. ^{1}H NMR: 3.96−3.91 (m, 3H), 3.81−3.76 (m, 1H), 3.66 (s, 3H), 3.27 (dd, J = 7.8, 6.1 Hz, 1H), 3.09 (dd, J = 9.7, 8.8 Hz, 1H), 2.60 (dd, J = 12.3, 9.7 Hz, 1H), 2.24 (s, 3H), 2.21 (dd, J = 12.3, 8.7 Hz, 1H), 2.14−2.08 (m, 1H), 1.86−1.81 (m, 1H), 1.75−1.50 (m, 4H). ^{13}C NMR: 210.6, 172.8, 108.6, 64.9, 64.5, 63.1, 53.4, 51.4, 36.3, 36.2, 31.3, 29.7, 28.2, 23.0. IR: 1733, 1702.

3-Methoxymethoxy-2-methyl-2-(2-oxopropyl)cyclobutanecarboxylic Acid Methyl Ester (37). The product from the basic treatment required heating in refluxing THF to undergo the retro-aldol reaction. The cycloadduct **25** (81 mg, 0.3 mmol) afforded (30 min) a 30:70 mixture of diastereomers **37a** and **37b** (56 mg, 77%) as a colorless oil after purification (Et_2O:PE = 1:4). Both isomers were obtained pure after repeated chromatography. **37a:** Colorless oil. R_f = 0.15. ^{1}H NMR: 4.55 (d, J = 6.6 Hz, 1H), 4.50 (d, J = 6.6 Hz, 1H), 3.74 (dd, J = 8.7, 7.4 Hz, 1H), 3.63 (s, 3H), 3.34 (s, 3H), 2.80 (d, J = 18 Hz, 1H), 2.64 (d, J = 18 Hz, 1H), 2.44 (dd, J = 10.8, 7.5 Hz, 1H), 2.34−2.24 (m, 2H), 2.11 (s, 3H), 1.44 (s, 3H). ^{13}C NMR: 207.2, 173.3, 96.7, 76.3, 55.3, 51.5, 48.8, 42.5, 40.6, 28.4, 26.1. IR: 1731. HRMS (FAB) calculated for $C_{12}H_{21}O_5$ (MH^+) 245.1389, found 245.1382. **37b:** Colorless oil. R_f = 0.10. ^{1}H NMR: 4.56 (d, J = 6.5 Hz, 1H), 4.53 (d, J = 6.5 Hz, 1H), 3.98 (ddd, J = 7.0, 5.2, 1.0 Hz, 1H), 3.68 (s, 3H), 3.32 (s, 3H), 3.01 (ddd, J = 9.3, 5.9, 1.0 Hz, 1H), 2.80 (d, J = 16.8 Hz, 1H), 2.68 (d, J = 16.8 Hz, 1H), 2.54 (ddd, J = 12.8, 7.1, 5.9 Hz, 1H), 2.15 (s, 3H), 2.01 (ddd, J = 12.7, 9.3, 5.2, 1H), 1.16 (s, 3H). ^{13}C NMR: 207.2, 173.9, 95.6, 77.3, 55.4, 51.4, 48.0, 46.0, 42.7, 31.4 27.3, 20.6. IR: 1733 (br).

3-Methoxymethoxy-2-(1-methyl-2-oxopropyl)cyclobutanecarboxylic Acid Methyl Ester (38). The cycloadduct mixture (70:20:10) **26** (22 mg, 0.08 mmol) afforded (45 min) a 70:30 mixture of two main diastereomers **38a** and **38b** (15 mg, 75%) as a colorless oil after purification (Et_2O:PE = 1:3). Both isomers were obtained pure after repeated chromatography. **Main isomer 38a:** Colorless oil. R_f = 0.12. ^{1}H NMR: 4.64 (d, J = 6.7 Hz, 1H), 4.56 (d, J = 6.7 Hz, 1H), 4.32−4.26 (m, 1H), 3.59 (s, 3H), 3.57 (s, 3H), 3.13−3.06 (m, 1H), 2.99 (ddd, J = 8.8, 7.9, 0.9 Hz, 1H), 2.38−2.34 (m, 2H), 2.17−2.14 (m, 1H), 2.15 (s, 3H), 1.13 (d, J = 7.0 Hz, 3H). ^{13}C NMR: 211.5, 174.3, 94.6, 70.5, 55.5, 51.4, 45.2, 42.9, 35.5, 30.7, 28.3, 16.3. IR: 1714, 1712. HRMS (FAB) calculated for $C_{12}H_{21}O_5$ (MH^+) 245.1389, found 245.1383. **38b:** Colorless oil. R_f = 0.08. ^{1}H NMR: 4.66 (d, J = 6.7 Hz, 1H), 4.53 (d, J = 6.7 Hz, 1H), 4.34 (ddt, J = 6.6, 2.3, 0.9 Hz, 1H), 3.67 (s, 3H), 3.37 (s, 1H), 3.03 (ddt, J = 9.1, 8.2, 0.9 Hz, 1H), 2.95 (dq, J = 10.6, 6.8 Hz, 1H), 2.88−2.82 (m, 1H), 2.35 (ddd, J = 12.5, 8.2, 1.0 Hz, 1H), 2.17−2.11 (m, 1H), 2.14 (s, 3H), 1.57 (s, 3H), 1.12 (d, J = 6.8, 3H). ^{13}C NMR: 211.2, 174.9, 94.5, 71.2, 55.6, 51.6, 46.0, 45.5, 40.0, 30.1, 28.3, 15.1. IR: 1734, 1711.

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Supporting Information Available: Copies of ^{1}H NMR spectra of diols **10** and **16**, cycloadducts **21**−**26**, **3**, and **4**, and tetraol **32**. Tables of X-ray crystallographic data of compounds **10**, **3**, **4**, and **35**. This material is available free of charge via the Internet at http://pubs.acs.org.

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