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[2+2] Photocycloaddition of Symmetrically Disubstituted Alkenes to 2(5*H*)-Furanones: Diastereoselective Entry to 1,2,3,4-Tetrasubstituted Cyclobutanes

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A study on the [2+2] photochemical cycloaddition of 1,4-difunctionalized 2-butenes to 2(5*H*)-furanones is presented. These reactions deliver 1,2,3,4-tetrasubstituted cyclobutanes with suitable functionalization in the four side chains for further synthetic elaboration. The effects of the substituents in both the lactone and the 2-butene on the stereoselectivity of the photochemical reaction have been evaluated. Starting from (*Z*)-2-butenes, under photosensitized conditions, a competitive *cis*/*trans* isomerization of the olefin inhibits the cycloaddition process. It was found that the presence of a *cis* double bond confined within a medium-size ring does not prevent bond rotation in the intermediate 1,4-biradicals.

Introduction

Nature synthesizes a variety of cyclobutane compounds in which the four positions of the ring are substituted. The majority of these compounds display bilateral symmetry due to a dimerization process that takes place during their biosynthesis. The most studied among these natural products is the alkaloid (–)-sceptrin (**1**), which was isolated from the sea sponge *Agelas Sceptrum* in 1981[1] and exhibits potent activity as an antiviral, antimuscarinic, antibacterial, and antihistaminic agent.[2] Recently, other 1,2,3,4-tetrasubstituted cyclobutanes have also been isolated from natural sources,[3] such as incarvilateine (**2**) from *Incarvillea sinensis*,[4] and dipiperamide A (**3**) from *Piper nigrum* (Figure 1).[5]

Despite the potent biological activity shown by sceptrin (**1**), only three synthetic approaches to this interesting compound have been described. In 2004, Birman and Jiang published the first synthesis of racemic **1**, where the key cyclobutane was constructed through a [2+2] photocycloaddition of maleic anhydride (**4**), to (*E*)-1,4-dichloro-2-butene [(*E*)-**5**],[6] (Scheme 1). The same year, Baran and co-workers disclosed another synthesis of racemic **1** using 2,5-dimethylfuran and dimethyl acetylenedicarboxylate as starting materials.[7] A modification of the latter approach by adding a desymmetrization step led to the first enantioselective preparation of (–)-sceptrin.[8]

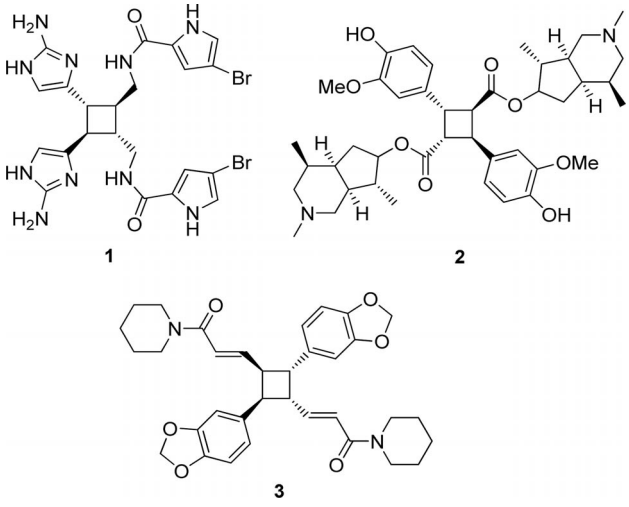
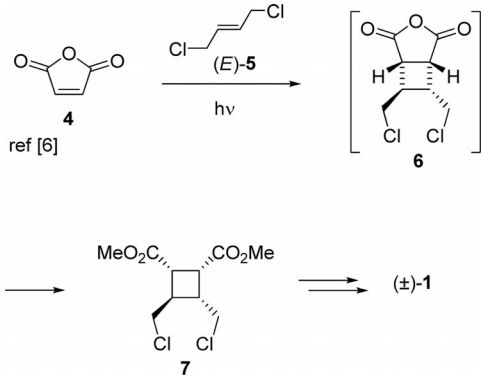


Figure 1. Tetrasubstituted natural cyclobutane compounds.



Scheme 1. [2+2] Photochemical reaction of maleic anhydride (**4**) and olefin (*E*)-**5** for the synthesis of (±)-sceptrin.

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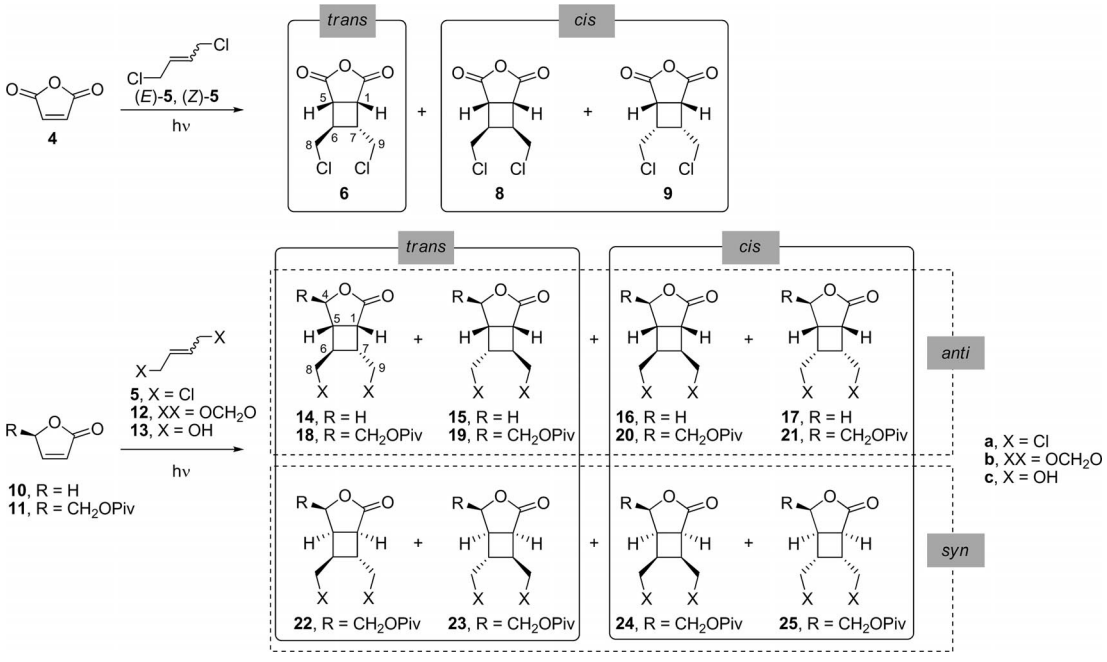
As part of our research program directed towards the preparation of natural products and analogues containing a cyclobutane ring,[9] we have studied in depth the [2+2] photochemical cycloaddition of 1,4-difunctionalized 2-butenes to 2(5*H*)-furanones as a means to prepare 1,2,3,4-tetrasubstituted cyclobutanes with suitable functionalization in the four side chains for further synthetic elaboration. We have evaluated the lactone and butene substituent effects on the stereoselectivity of the photochemical reaction, as well as the photoexcitation effect on the reactivity and its influence on the side processes. The use of a chiral lactone as the substrate gives access to enantiopure cyclobutane derivatives, which might be useful precursors of the bioactive compound (–)-sceptrin and other interesting natural products.

Results and Discussion

Chiral 2(5*H*)-furanone **11** was prepared from 1,2:5,6-di-*O*-isopropylidene-D-mannitol according to a previously reported methodology.[10] Selection of the protecting group was guided by the excellent results obtained by our group in the [2+2] photocycloaddition of **11** to ethylene derivatives.[11] Literature precedents for the use of symmetrical 2-butenes in photocycloadditions to enones were limited to achiral substrates.[12] Therefore, the inclusion of a stereogenic center as in **11** entailed overcoming a new challenge. Birman and Jiang described that, upon irradiation through a Pyrex filter of a solution of maleic anhydride (**4**) and benzophenone in (*E*)-1,4-dichloro-2-butene [(*E*)-**5**], the *trans* cycloadduct **6** was apparently formed as the only product; after methanolysis, this compound delivered diester **7** in 76% yield (Scheme 1). In our hands, this photoreaction, performed under exactly the same conditions, furnished an 85:10:5 mixture of **6** and the *cis* cycloadducts **8** (*endo*) and **9** (*exo*), in overall 71% yield (Scheme 2). The photochemical reaction between **4** and (*E*)-**5** was also performed using our own photochemical methodology, which was systemically applied to the complete study. Thus, substrates **4**, **10**, or **11** and a ninefold excess of 2-butenes **5**, **12**, or **13** in either acetonitrile or acetone solutions, were irradiated through a Quartz or Pyrex filter using a 125 W high-pressure mercury lamp at 0 °C. The progress of the cycloaddition was monitored by either GC or ^{1}H NMR analysis, and the irradiation was prolonged until the conversion remained constant. The results are listed in Table 1.

To compare our results with the literature precedents, anhydride maleic (**4**), and (*E*)- and (*Z*)-1,4-dichloro-2-butene, (*E*)-**5** and (*Z*)-**5**, were first investigated (Table 1, entries 1–4). When the irradiation was performed through a Quartz filter, in both cases, a mixture of the three possible cycloadducts **6**, **8**, and **9** was formed in similar yield and a comparable ratio, with the *trans* cycloadduct **6** being the predominant isomer. When the irradiation was performed through a Pyrex filter, similar results were found starting from (*E*)-**5**, but (*Z*)-**5** did not furnish the expected cycloadducts and the only process observed in this case was isomerization to (*E*)-**5**. Chromatographic separation of cycloadducts **6/8/9** was not possible due to their degradation upon contact with silica gel, therefore, for identification purposes, it was necessary to perform NMR analyses of samples containing a mixture of isomers. The C-6/C-7 *trans* configuration of the major cycloadduct **6** was assigned on the basis of a NOESY experiment, which showed cross-peaks between the protons at C-8 and the cyclobutane proton H-7, and between the protons at C-9 and the cyclobutane proton H-6. This assignment was corroborated by the higher field shift of C-9 in the ^{13}C NMR spectra compared to that of



Scheme 2. [2+2] Photochemical reaction of lactones **4**, **10**, and **11** with 2-butenes **5**, **12**, and **13**.

Table 1. [2+2] Photocycloaddition reaction of lactones **4**, **10**, and **11** to 2-butenes **5**, **12**, and **13**.

Entry	Enone	Butene	Filter	Solvent	*t* [h]	Yield [%][b]	Products[e]	Ratio[g]	*anti*/*syn*	*trans*/*cis*[i]
1	**4**	(*E*)-**5**	quartz	acetonitrile	1.5	75[c]	**6**, **8**, **9**	88:9:3	–	7.3:1
2	**4**	(*E*)-**5**	pyrex	acetone	4	71[c]	**6**, **8**, **9**	86:9:5	–	6.1:1
3	**4**	(*Z*)-**5**	quartz	acetonitrile	4	73[c]	**6**, **8**, **9**	83:9:8	–	4.9:1
4	**4**	(*Z*)-**5**	pyrex	acetone	4	–	–	–	–	–
5	**10**	(*E*)-**5**	quartz	acetonitrile	9	58 (83)[d]	**14a**, **15a**, **16a**, **17a**	34:30:23:13	–	1.8:1
6	**10**	(*E*)-**5**	pyrex	acetone	11	44 (75)[d]	**14a**, **15a**, **16a**, **17a**	37:28:23:12	–	1.9:1
7	**10**	(*Z*)-**5**	quartz	acetonitrile	10	46 (87)[d]	**14a**, **15a**, **16a**, **17a**	35:25:29:11	–	1.5:1
8	**10**	(*Z*)-**5**	pyrex	acetone	10	–	–	–	–	–
9	**11**	(*E*)-**5**	quartz	acetonitrile	4	68 (91)[d]	**18a**, **19a**, **23a**	40:33:27	2.7:1	1:0
10	**10**	(*Z*)-**12**[a]	quartz	acetonitrile	3.5	70 (84)[d]	**16b**, **14b**, **15b**	70:15:15	–	1:2.3
11	**10**	(*Z*)-**12**	pyrex	acetone	6	–	–	–	–	–
12	**11**	(*Z*)-**12**	quartz	acetonitrile	4	70 (77)[d]	**20b**, **25b**, **19b**, **18b**	54:15:14:17	5.7:1	1:2.2
13	**10**	(*Z*)-**13**[a]	quartz	acetonitrile	3	69 (81)[d]	**16c**, **14c**, **15c**	46:35:19[h]	–	1.2:1
14	**10**	(*Z*)-**13**	pyrex	acetone	4	35 (78)[d]	**16c**, **14c**, **15c**	43:37:20[h]	–	1.3:1
15	**11**	(*Z*)-**13**	quartz	acetonitrile	4	46 (69)[d]	**18c**, **19c**, **C**[f]	46:38:16	–	–

[a] The *E* isomer is not commercially available. [b] Isolated yield of the mixture of stereoisomers after column chromatography except for entries 1–4. [c] Isolated yield of the mixture of stereoisomers after removal of the excess of olefin **5** by kugelrohr distillation. [d] Isolated yield considering the starting material recovered is given in parenthesis. [e] Products given in order of time retention on a GC column. [f] The third diastereoisomer **C** could not be fully characterized. [g] Isomer ratio from GC analysis of the crude reaction mixture. [h] Isomer ratio from ^{13}C NMR analysis of the crude reaction mixture. [i] C-6/C-7 relative configuration.

C-8, which was connected to the larger steric compression of the former.

The photoreaction of crotonolactone (**10**), with (*E*)- and (*Z*)-**5** in acetonitrile using a Quartz filter (Table 1, entries 5 and 7) rendered, in moderate yields, the four possible cycloadducts **14a**, **15a**, **16a**, and **17a** with a poor C-6/C-7 *trans*/*cis* ratio of 1.8:1 and 1.5:1, respectively, which was determined by NOESY experiments and further corroborated by the value of the coupling constant between H-6 and H-7. The relative configuration between H-5 and H-6 was inferred from the chemical shift of C-4 in the ^{13}C NMR spectra. Thus, the signal of C-4 is high-field shifted when this carbon atom is close to the bulky chloromethyl group, namely, when H-5 and H-6 are in a *cis* relationship. Cross-peaks on the NOESY experiments between H-4 and H-6 in the 5,6-*cis* cycloadducts, and between H-4 and H-8 in the 5,6-*trans* cycloadducts validated the diagnostic value of the above parameter. When the reaction with **10** was assayed through a Pyrex filter in acetone as solvent and sensitizing agent (Table 1, entries 6 and 8), olefin (*E*)-**5** lead to the formation of four expected cycloadducts **14a**–**17a** in a 1.9:1, 6,7-*trans*/*cis* ratio and 46% yield, while the (*Z*)-**5** isomer did not react. Similar to the case of maleic anhydride, instead of the photocycloaddition, an isomerization from the (*Z*)-olefin to (*E*)-**5** was again observed as the only process.

In view of the above results, we wanted to examine the effect of acetone and crotonolactone (**10**) as potential sensitizing agents for the *E*/*Z* isomerization of **5** (Table 2). When (*E*)-**5** was irradiated, the isomerization of the double bond was not observed in any of the four sets of conditions assayed (Table 2, entries 1–4). In contrast, when (*Z*)-**5** was irradiated, isomerization was observed in the presence of either acetone (Table 2, entry 6), crotonolactone (**10**) (entry 7) or both (entry 8). These results may be explained by considering various mechanistic alternatives. Firstly, a photosensitized process may occur that transfers the energy from the triplet of acetone and/or the triplet of **10** to (*Z*)-**5**, hence inducing its excitation to an orthogonal triplet state that can undergo relaxation to either isomer of the olefin.[13] It is also plausible that the triplet state of acetone (Table 2, entry 6) or crotonolactone (entry 8) reacted with olefin (*Z*)-**5**, but the intermediate biradical species did not evolve to the oxetane[14] or cyclobutane adducts because reversion to the starting carbonyl compound and the olefin (*Z* or *E*) was more favored.[15] Because the newly formed olefin (*E*)-**5** is unable to react with crotonolactone to furnish the cycloadducts, it must be concluded that these competitive pathways inhibit the photocycloaddition process.

Table 2. Study of the of *E*/*Z* photoisomerization of **5**.

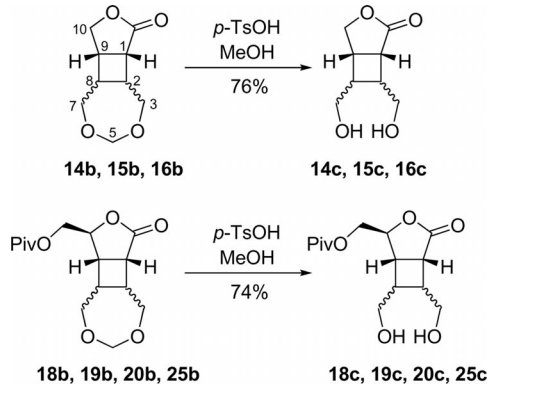
Entry	Olefin	Filter	Solvent	Substrate	*Z*/*E*[c]
1	(*E*)-**5**[a]	quartz	acetonitrile	–	1:32
2	(*E*)-**5**	pyrex	acetone	–	1:32
3	(*E*)-**5**	quartz	acetonitrile	**10**	1:32
4	(*E*)-**5**	pyrex	acetone	**10**	1:32
5	(*Z*)-**5**[b]	quartz	acetonitrile	–	19:1
6	(*Z*)-**5**	pyrex	acetone	–	1:2.3
7	(*Z*)-**5**	quartz	acetonitrile	**10**	4.9:1
8	(*Z*)-**5**	pyrex	acetone	**10**	2.1:1

[a] Commercial (*E*)-**5** is contaminated with 3% of the *Z* isomer (*Z*/*E* ratio 1:32). [b] Commercial (*Z*)-**5** is contaminated with 5% of the *E* isomer (*Z*/*E* ratio 19:1). [c] Isomer ratio determined by GC analysis of the crude reaction mixture after 2 h of irradiation.

Once the reaction of butene **5** with the achiral substrates **4** and **10** had been investigated, the best synthetic conditions were applied to the enantiopure 2(5*H*)-furanone **11** (Table 1, entry 9). Considering the mechanistic proposal for this kind of photocycloaddition that postulates free rotation of the C-6/C-7 bond on the 1,4-biradical intermediates,[15] this reaction could lead to the formation of up to eight products, which can be classified into four different pairs: *anti*/*trans*, *anti*/*cis*, *syn*/*trans*, and *syn*/*cis* (Scheme 2). Remarkably, irradiation of **11** in the presence of (*E*)-**5** in acetonitrile through a Quartz filter provided exclusively three cy-

cloadducts (**18a**, **19a**, and **23a**) in 68% overall yield. The C-6/C-7 *trans*/*cis* relative configuration was determined following the same method used for **14a**/**17a**. The disposition between H-4 and H-5 was assigned on the basis of the value of their coupling constant, which was lower for the *anti* (0 Hz for **18a** and 1.7 Hz for **19a**) than for the *syn* cycloadducts (5.2 Hz for **23a**); the results were corroborated by NOESY experiments. Because the three isolated isomers present C-6/C-7 *trans* relative configuration, all of them are attractive precursors for the synthesis of enantiopure 1,2,3,4-tetrasubstituted cyclobutanes with all the neighbor substituents in a *trans* disposition, as in sceptrin (**1**). Specifically, **18a** could lead to the natural alkaloid (–)-**1**, and **19a** and **23a** to the non natural sceptrin (+)-**1**, following the route described by Birman and Jiang for the synthesis of the racemate.

To explore the possibility of achieving C-6/C-7 *cis* cycloadducts, we investigated the [2+2] photocycloaddition of 2(5*H*)-furanones **10** and **11** to (*Z*)-4,7-dihydro-1,3-dioxepin [(*Z*)-**12**], expecting that the occurrence of a more rigid cyclic moiety may prevent bond rotation in the intermediate 1,4-biradical species. The photoreaction of **10** and (*Z*)-**12** using a Quartz filter without a sensitizing agent, furnished a 15:15:70 mixture of **14b**, **15b**, and **16b** in 70% total yield (Table 1, entry 10), showing that the cyclic nature of the olefin does not entirely preclude C-6/C-7 bond rotation, although the predominating isomer of the product displays *cis* relative configuration, as expected. In a parallel experiment, carried out in acetone using a Pyrex filter (Table 1, entry 11), most of the starting material was recovered unchanged. Consequently, only the first protocol was applied to lactone **11** (Table 1, entry 12), resulting in the formation of a mixture of four among the eight possible diastereomers in a 1:2.2 C-6/C-7 *trans*/*cis* ratio, from which the major cycloadduct could be isolated in 54% yield. The relative configuration of the new stereogenic centers was determined by the value of the coupling constants $J_{1,2}$ and $J_{8,2}$ (numbering shown in Scheme 3). Other useful data for the stereochemical assignment was the chemical shift of the diastereotopic protons at C-5, which are isochronous when the four- and seven-member rings are *trans* fused, and display an AB system with approximately 1 ppm separation when these two rings are *cis* fused. For **18b**, **19b**, **20b**, and **25b**, the *anti*/*syn* configuration was assigned through the coupling constant $J_{9,10}$. All the stereochemical assignments were confirmed by NOESY experiments. To extend their synthetic utility, the mixture of oxepanes derived from either lactone were converted into the corresponding diols by treatment with *p*TsOH in MeOH (Scheme 3).



Scheme 3. Methanolysis of the acetal to furnish the diol derivatives.

To complete the photochemical study, lactones **10** and **11** were irradiated in the presence of (*Z*)-2-buten-1,4-diol [(*Z*)-**13**], which is more readily available than its *E* isomer (Table 1, entries 13–15). The photoreaction with achiral furanone **10** in acetonitrile using a Quartz filter delivered three isomeric cycloadducts **14c**–**16c** in 69% isolated yield, with a slight predominance of the C-6/C-7 *trans* relative configuration. The same products in a similar proportion were also formed when the irradiation was carried out in acetone through a Pyrex filter, but, under these conditions, the yield decreased to 35%. We believe that this loss of effectiveness when the cycloaddition is performed under photosensitized conditions may be related to the existence of a competitive *cis*/*trans* isomerization process of the olefin, as was observed for (*Z*)-**5**, although in this case the corresponding *trans* isomer (*E*)-**13** was not detected. Finally, direct irradiation conditions were applied to chiral furanone **11**, providing a mixture of three cycloadducts, although only two could be identified (**18c** and **19c**) due to severe difficulties encountered in the chromatographic purification of the crude material. The relative configuration of **14c**–**16c**, **18c**, and **19c** was assigned as described above for the chlorinated cycloadducts and by correlation with the dioxepane derivatives through methanolysis.

Conclusions

It has been found that the [2+2] photocycloaddition of 2(5*H*)-furanones to 1,4-difunctionalized 2-butenes works well upon direct irradiation of an acetonitrile solution of the reactants through a Quartz filter. Starting from (*Z*)-2-butenes, under photosensitized conditions, a competitive *cis*/*trans* isomerization of the olefin inhibits the cycloaddition process. From a synthetic point of view, the most useful of the studied reactions was the photocycloaddition of chiral furanone **11** to *trans* dichlorobutene (*E*)-**5**, leading exclusively to C-6/C-7 *trans*-cyclobutanes, which can be appropriate precursors for the enantioselective synthesis of natural 1,2,3,4-tetrasubstituted cylobutanes such as sceptrin (**1**), and others. Photocycloadditions performed with 1,3-dioxepin (*Z*)-**12** provided evidence that the presence of a *cis* double bond confined within a medium-size ring does not prevent bond rotation in the intermediate 1,4-biradicals, although the sense of stereoselectivity is inverted from C-6/C-7 *trans* to *cis*. Work is in progress to develop synthetic applications of these photochemical reactions.

Experimental Section

General: Commercially available reagents were used as received. Solutions were concentrated using an evaporator at 15–20 Torr.

Flash column chromatography separations were carried out on silica gel (230–400 mesh). Melting points were determined on a hot stage apparatus. ^{1}H and ^{13}C NMR spectra were recorded at the Servei de Ressonància Magnètica Nuclear de la Universitat Autònoma de Barcelona at 250 and 62.5 MHz, 360 and 90 MHz, or 400 and 100 MHz. NMR signals were assigned with the help of DEPT, COSY, HMBC, and HMQC experiments. High resolution mass spectra (HRMS) and Microanalyses were performed at the Servei d'Anàlisi Química de la Universitat Autònoma de Barcelona. Optical rotations were measured at 22 ± 2 °C.

(1*RS*,5*SR*,6*SR*,7*SR*)-6,7-Bis(chloromethyl)-3-oxabicyclo[3.2.0]-heptan-2,4-dione (6), (1*RS*,5*SR*,6*SR*,7*RS*)-6,7-Bis(chloromethyl)-3-oxabicyclo[3.2.0]heptan-2,4-dione (8) and (1*RS*,5*SR*,6*RS*,7*RS*)-6,7-Bis(chloromethyl)-3-oxabicyclo[3.2.0]heptan-2,4-dione (9). Birman and Jiang Methodology: An oxygen-free solution of maleic anhydride (**4**; 105 mg, 1.07 mmol) and benzophenone (49 mg, 0.27 mmol) in (*E*)-1,4-dichloro-2-butene [(*E*)-**5**; 1.25 g, 10.0 mmol] was placed in an NMR tube. This solution was irradiated through a Pyrex filter for 60 h at room temperature under a nitrogen atmosphere. The progress of the reaction was monitored by GC analysis. Evaporation of the solvent and kugelrohr distillation of (*E*)-**5** under reduced pressure afforded a mixture of **6**, **8** and **9** (86:9:5 ratio; 169 mg, 0.76 mmol, 71% yield). The cycloadducts **6**, **8**, and **9** decomposed upon contact with silica gel.

Compound 6: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 3.82 (m, 2 H, 8-H), 3.74 (m, 2 H, 9-H), 3.59 (m, 1 H, 1-H), 3.46 (m, 1 H, 5-H), 3.23 (m, 1 H, 7-H), 2.96 (m, 1 H, 6-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 171.0 (C=O), 170.0 (C=O), 46.1 (CH_2, 8-C), 43.8 (CH, 6-C), 43.5 (CH_2, 9-C), 39.5/39.2/38.9 (3×CH, 1-C/5-C/7-C) ppm. MS: *m*/*z* (%) = 180 (1.5), 178 (2.5), 152 (11), 150 (17), 117 (20), 115 (66), 103 (17), 101 (49), 79 (100).

Compound 8: MS: *m*/*z* (%) = 180 (2.0), 178 (3.1), 152 (7.5), 150 (12), 117 (16), 115 (50), 103 (18), 101 (50), 79 (100).

Compound 9: MS: *m*/*z* (%) = 180 (1.9), 178 (3.3), 152 (8), 150 (12), 117 (18), 115 (52), 103 (22), 101 (48), 79 (100).

General Procedure for Photochemical Reactions: The irradiation was performed in a small, conventional photochemical reactor (two-necked vessel fitted with a Quartz or Pyrex immersion-type cooling jacket) using a high pressure 125 W mercury lamp (Cathodeon HPK-125). Methanol at –15 °C was used to refrigerate the immersion well jacket. The vessel was externally cooled to 0 °C. The reaction mixture was initially degassed by passage of oxygen-free nitrogen through the solution for 10 min and then irradiated under an atmosphere of nitrogen. The progress of the reaction was monitored by GC or by ^{1}H or ^{13}C NMR analyses of sample aliquots.

Compounds 6, 8, and 9: A solution of maleic anhydride (**4**; 150 mg, 1.53 mmol) and (*E*)-1,4-dichloro-2-butene [(*E*)-**5**; 1.721 g, 13.8 mmol] in acetonitrile (90 mL) was irradiated through a Quartz filter for 1.5 h. The progress of the reaction was monitored by GC analysis. Evaporation of the solvent and kugelrohr distillation of (*E*)-**5** under reduced pressure afforded a mixture of **6**, **8**, and **9** (88:9:3 ratio; 255 mg, 1.14 mmol, 75% yield).

(1*RS*,5*SR*,6*RS*,7*RS*)-6,7-Bis(chloromethyl)-3-oxabicyclo[3.2.0]-heptan-2-one (14a), (1*RS*,5*SR*,6*SR*,7*SR*)-6,7-Bis(chloromethyl)-3-oxabicyclo[3.2.0]heptan-2-one (15a), (1*RS*,5*SR*,6*RS*,7*SR*)-6,7-Bis(chloromethyl)-3-oxabicyclo[3.2.0]heptan-2-one (16a), and (1*RS*,5*SR*,6*SR*,7*RS*)-6,7-Bis(chloromethyl)-3-oxabicyclo[3.2.0]-heptan-2-one (17a): A solution of 2(5*H*)-furanone **10** (150 mg, 1.78 mmol) and (*E*)-**5** (2.00 g, 16.0 mmol) in acetonitrile (90 mL) was irradiated through a Quartz filter for 9 h. The progress of the reaction was monitored by GC analysis. Evaporation of the solvent and column chromatography (hexane/EtOAc, 10:1) rendered a mixture of **14a**, **15a**, **16a**, and **17a** (34:30:23:13 ratio; 217 mg, 1.03 mmol, 58% yield) and unreacted lactone (37 mg, 0.44 mmol). Repeated column chromatography (hexane to hexane/EtOAc, 3:1) provided an oily residue, which was identified as pure **14a**, and enriched fractions of compounds **15a**–**17a**.

Compound 14a: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 4.41 (ddd, $^2J_{H,H}$ = 9.7, $^3J_{H,H}$ = 5.9, J = 1.2 Hz, 1 H, 4-H), 4.32 (br. d, $^2J_{H,H}$ = 9.7 Hz, 1 H, 4-H), 3.85 (dd, $^2J_{H,H}$ = 11.2, $^3J_{H,H}$ = 4.6 Hz, 1 H, 8-H), 3.75 (ddd, $^2J_{H,H}$ = 11.4, $^3J_{H,H}$ = 5.8, $^4J_{H,H}$ = 0.9 Hz, 1 H, 9-H), 3.62 (ddd, $^2J_{H,H}$ = 11.2, $^3J_{H,H}$ = 8.3, $^4J_{H,H}$ = 0.8 Hz, 1 H, 8-H), 3.50 (ddd, $^2J_{H,H}$ = 11.4, $^3J_{H,H}$ = 10.1, $^4J_{H,H}$ = 0.8 Hz, 1 H, 9-H), 3.22 (dd, $^3J_{H,H}$ = 9.4, 7.6 Hz, 1 H, 1-H), 2.96 (ddd, $^3J_{H,H}$ = 7.6, 6.0, 5.9 Hz, 1 H, 5-H), 2.82 (m, 1 H, 7-H), 2.55 (m, 1 H, 6-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 176.2 (C=O), 73.0 (CH_2, 4-C), 46.7 (CH_2, 8-C), 46.6 (CH, 6-C), 44.2 (CH_2, 9-C), 39.6 (CH, 7-C), 38.0 (CH, 1-C), 36.1 (CH, 5-C) ppm. IR (ATR): $\tilde{\nu}$ = 2960, 2907, 1757, 1477, 1261, 1161, 1042 cm^{-1}. MS *m*/*z* (%) = 208 (0.4) [M]$^+$, 175 (14), 173 (40), 85 (94), 67 (100). HRMS (ESI$^+$): calcd. for $C_8H_{10}Cl_2O_2Na$ 230.9950; found 230.9950.

Compound 15a: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 4.58 (dd, $^2J_{H,H}$ = 10.7, $^3J_{H,H}$ = 2.4 Hz, 1 H, 4-H), 4.43 (dd, $^2J_{H,H}$ = 10.7, $^3J_{H,H}$ = 8.2 Hz, 1 H, 4-H), 3.74 (m, 2 H, 9-H), 3.74–3.65 (m, 2 H, 8-H), 3.30 (dtd, $^3J_{H,H}$ = 8.2, 8.0, 2.4 Hz, 1 H, 5-H), 3.03 (dd, $^3J_{H,H}$ = 8.2, 4.7 Hz, 1 H, 1-H), 2.86 (m, 1 H, 6-H), 2.56 (m, 1 H, 7-H) ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 178.1 (C=O), 67.9 (CH_2, 4-C), 46.9 (CH_2, 9-C), 43.8 (CH, 7-C), 42.9 (CH_2, 8-C), 39.7 (CH, 6-C), 37.9 (CH, 1-C), 32.3 (CH, 5-C) ppm. MS *m*/*z* (%) = 208 (0.1) [M]$^+$, 175 (3.5), 173 (11), 85 (100).

Compound 16a: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 4.41 (dd, $^2J_{H,H}$ = 9.7, $^3J_{H,H}$ = 5.9 Hz, 4-H), 4.32 (dd, $^2J_{H,H}$ = 9.7, $^3J_{H,H}$ = 1.0 Hz, 4-H), 3.88–3.60 (m, 4 H, 2× 8-H, 2× 9-H), 3.12–2.76 (m, 4 H, 1-H, 5-H, 6-H, 7-H) ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 178.1 (C=O), 72.8 (CH_2, 4-C), 43.6/43.2 (CH/CH_2, 6-C/8-C), 42.8 (CH_2, 9-C), 41.3 (CH), 38.9 (CH), 38.2 (CH) ppm. MS: *m*/*z* (%) = 208 (0.5) [M]$^+$, 175 (13), 173 (41), 85 (100).

Compound 17a: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 4.55–4.10 (m, 2 H, 2× 4-H), 3.84–3.58 (m, 4 H, 2× 8-H, 2× 9-H), 3.21–2.98 (m, 2 H, 1-H, 5-H), 2.50–2.20 (m, 2 H, 6-H, 7-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 178.6 (C=O), 63.5 (CH_2, 4-C), 45.6 (CH_2), 45.6 (CH_2), 40.5 (CH), 39.7 (CH), 31.1 (CH), 29.1 (CH) ppm. MS: *m*/*z* (%) = 175 (0.3), 173 (2.7), 85 (100). Mixture **15a**–**16a**: HRMS (ESI$^+$): calcd. for $C_8H_{10}Cl_2O_2Na$ 230.9950; found 230.9945.

Irradiation of a solution of lactone **10** (150 mg, 1.78 mmol) and (*E*)-**5** (2.00 g, 16.0 mmol) in acetone (90 mL) through a Pyrex filter for 11 h furnished a mixture of **14a**, **15a**, **16a**, and **17a** (37:28:23:12 ratio; 165 mg, 0.79 mmol, 44% yield) and unreacted lactone (46 mg, 0.55 mmol) after purification of the crude material by silica gel column chromatography.

Irradiation of a solution of lactone **10** (150 mg, 1.78 mmol) and (*Z*)-**5** (2.00 g, 16.0 mmol) in acetonitrile (90 mL) through a Quartz filter for 10 h furnished a mixture of **14a**, **15a**, **16a**, and **17a** (35:25:29:11 ratio; 171 mg, 0.82 mmol, 46% yield) and unreacted lactone (61 mg, 0.73 mmol) after purification of the crude material by silica gel column chromatography.

Irradiation of a solution of lactone **10** (150 mg, 1.78 mmol) and (*Z*)-**5** (2.00 g, 16.0 mmol) in acetone (90 mL) through a Pyrex filter for 10 h delivered the unreacted lactone **10** (135 mg, 1.60 mmol)

after purification of the crude material by silica gel column chromatography.

(1*S*,4*S*,5*R*,6*S*,7*S*)-6,7-Bis(chloromethyl)-4-(pivaloyloxymethyl)-3-oxabicyclo[3.2.0]heptan-2-one (18a), (1*S*,4*S*,5*R*,6*R*,7*R*)-6,7-Bis(chloromethyl)-4-(pivaloyloxymethyl)-3-oxabicyclo[3.2.0]heptan-2-one (19a), and (1*R*,4*S*,5*S*,6*S*,7*S*)-6,7-Bis(chloromethyl)-4-(pivaloyloxymethyl)-3-oxabicyclo[3.2.0]heptan-2-one (23a): A solution of (*S*)-5-(pivaloyloxymethyl)-2(5*H*)-furanone (**11**; 150 mg, 0.76 mmol) and (*E*)-**5** (856 mg, 6.84 mmol) in acetonitrile (90 mL) was irradiated through a Quartz filter for 4 h. The progress of the reaction was monitored by GC analysis. Evaporation of the solvent and column chromatography of the residue (hexane/EtOAc, 10:1 to 6:1) rendered a mixture of **18a**, **19a**, and **23a** (40:33:27 ratio; 166 mg, 0.51 mmol, 68% yield) and unreacted starting material **11** (34 mg, 0.17 mmol). Repeated column chromatography (hexane to hexane/EtOAc, 6:1) furnished the following fractions: (i) an oil identified as pure **18a**; (ii) an enriched fraction of **19a**, and (iii) an enriched fraction of **23a**.

Compound 18a: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 4.65 (dd, $^3J_{H,H}$ = 3.4, 3.1 Hz, 1 H, 4-H), 4.25 (dd, $^2J_{H,H}$ = 12.2, $^3J_{H,H}$ = 3.4 Hz, 1 H, CH_2OPiv), 4.12 (dd, $^2J_{H,H}$ = 12.2, $^3J_{H,H}$ = 3.1 Hz, 1 H, CH_2OPiv), 3.86 (dd, $^2J_{H,H}$ = 11.2, $^3J_{H,H}$ = 4.6 Hz, 1 H, 8-H), 3.75 (dd, $^2J_{H,H}$ = 11.3, $^3J_{H,H}$ = 5.6 Hz, 1 H, 9-H), 3.60 (dd, $^2J_{H,H}$ = 11.2, $^3J_{H,H}$ = 8.6 Hz, 1 H, 8-H), 3.49 (dd, $^2J_{H,H}$ = 11.3, $^3J_{H,H}$ = 10.2 Hz, 1 H, 9-H), 3.27 (dd, $^3J_{H,H}$ = 9.5, 7.3 Hz, 1 H, 1-H), 2.82 (m, 1 H, 7-H), 2.81 (dd, $^3J_{H,H}$ = 7.3, 6.4 Hz, 1 H, 5-H), 2.57 (m, 1 H, 6-H), 1.19 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 177.8 (C=O, lactone), 175.2 (C=O, ester), 81.8 (CH, 4-C), 65.0 (CH_2, *C*H_2OPiv), 46.6/46.5 (CH/CH_2, 6-C/8-C), 44.2 (CH_2, 9-C), 40.1 (CH, 7-C), 39.0 (CH, 1-C), 38.8 [$(CH_3)_3$*C*], 38.5 (CH, 5-C), 27.1 [(*C*H_3)$_3$C] ppm. IR (ATR): $\tilde{\nu}$ = 2962, 2872, 1770, 1724, 1479, 1283, 1145, 1086 cm^{-1}. MS *m*/*z* (%) = 289 (1.4), 287 (4.1), 222 (5), 220 (7), 57 (100). $C_{14}H_{20}Cl_2O_4$ (323.22): calcd. C 52.02, H 6.24; found C 52.19, H 6.49.

Compound 19a: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 4.98 (ddd, $^3J_{H,H}$ = 3.4, 3.1, 1.7 Hz, 1 H, 4-H), 4.31 (dd, $^2J_{H,H}$ = 12.1, $^3J_{H,H}$ = 3.1 Hz, 1 H, CH_2OPiv), 4.15 (dd, $^2J_{H,H}$ = 12.1, $^3J_{H,H}$ = 3.5 Hz, 1 H, CH_2OPiv), 3.77–3.64 (m, 4 H, 2× 8-H, 2× 9-H), 3.09 (m, 2 H, 1-H, 5-H), 2.93 (m, 1 H, 6-H/7-H), 2.58 (m, 1 H, 6-H/7-H), 1.19 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 177.8 (C=O, lactone), 177.1 (C=O, ester), 76.7 (CH, 4-C), 65.8 (CH_2, *C*H_2OPiv), 46.8, 43.7, 42.9, 39.7, 39.0, 38.8 [$(CH_3)_3$*C*], 35.0, 27.1 [(*C*H_3)$_3$C] ppm. MS: *m*/*z* (%) = 289 (1.2), 287 (3.4), 222 (0.8), 220 (1.0), 57 (100).

Compound 23a: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 4.72 (td, $^3J_{H,H}$ = 6.0, 5.2 Hz, 1 H, 4-H), 4.39–4.35 (m, 2 H, CH_2OPiv), 3.78 (m, 1 H, 8-H), 3.74 (m, 1 H, 9-H), 3.62 (dd, $^2J_{H,H}$ = 11.3, $^3J_{H,H}$ = 6.9 Hz, 1 H, 8-H), 3.51 (dd, $^2J_{H,H}$ = 11.4, $^3J_{H,H}$ = 9.5 Hz, 1 H, 9-H), 3.30 (dd, $^3J_{H,H}$ = 8.1, 7.4 Hz, 1 H, 1-H), 3.04 (ddd, $^3J_{H,H}$ = 7.4, 5.3, 5.2 Hz, 1 H, 5-H), 2.84 (m, 1 H, 7-H), 2.75 (m, 1 H, 6-H), 1.22 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 178.0 (C=O, lactone), 174.9 (C=O, ester), 78.6 (CH, 4-C), 62.4 (CH_2, *C*H_2OPiv), 46.4 (CH_2, 8-C), 44.1 (CH_2, 9-C), 41.1 (CH, 6-C), 39.7 (CH, 1-C), 39.3 (CH, 7-C), 38.9 [$(CH_3)_3$ *C*], 38.0 (CH, 5-C), 27.1 [(*C*H_3)$_3$C] ppm. MS: *m*/*z* (%) = 289 (1.6), 287 (4.6), 222 (5), 220 (8), 57 (100).

Mixture of **18a**, **19a** and **23a**: HRMS (ESI$^+$): calcd. for $C_{14}H_{20}Cl_2O_4Na$ 345.06309; found 345.06303.

(1*RS*,2*SR*,8*RS*,9*SR*)-4,6,11-Trioxatricyclo[7.3.0.0^{2,8}]dodecan-12-one (16b), (1*RS*,2*RS*,8*RS*,9*SR*)-4,6,11-Trioxatricyclo[7.3.0.0^{2,8}]dodecan-12-one (14b), and (1*RS*,2*SR*,8*SR*,9*SR*)-4,6,11-Trioxatricyclo[7.3.0.0^{2,8}]dodecan-12-one (15b): A solution of 2(5*H*)-furanone **10** (150 mg, 1.78 mmol) and (*Z*)-**12** (1.602 g, 16.0 mmol) in acetonitrile (90 mL) was irradiated through a Quartz filter for 3.5 h. The progress of the reaction was monitored by GC analysis, where the appearance of three new peaks was observed (70:15:15). Evaporation of the solvent and column chromatography over silica gel (hexane/EtOAc, 1:1) provided the following fractions: (i) a white solid identified as **16b** (160 mg, 0.87 mmol, 49% yield), (ii) a white solid identified as a mixture of **14b** and **15b** (1:1 ratio; 68 mg, 0.37 mmol, 21% yield), and (iii) unreacted lactone (21 mg, 0.25 mmol).

Compound 16b: M.p. 93–95 °C (EtOAc/pentane). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 5.19 (d, $^2J_{H,H}$ = 7.3 Hz, 1 H, 5-H), 4.37 (d, $^2J_{H,H}$ = 7.3 Hz, 1 H, 5-H), 4.40 (dd, $^2J_{H,H}$ = 9.7, $^3J_{H,H}$ = 6.8 Hz, 1 H, 10-H), 4.26 (dd, $^2J_{H,H}$ = 9.7, $^3J_{H,H}$ = 1.5 Hz, 1 H, 10-H), 4.17 (dd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 2.9 Hz, 1 H, 3-H), 3.99 (dd, $^2J_{H,H}$ = 13.5, $^3J_{H,H}$ = 3.7 Hz, 1 H, 7-H), 3.79 (dd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 2.2 Hz, 1 H, 3-H), 3.68 (dd, $^2J_{H,H}$ = 13.5, $^3J_{H,H}$ = 1.3 Hz, 1 H, 7-H), 3.37 (ddd, $^3J_{H,H}$ = 8.2, 6.8, 5.6 Hz, 1 H, 9-H), 3.10 (dd, $^3J_{H,H}$ = 8.2, 3.5 Hz, 1 H, 1-H), 2.74 (m, 1 H, 8-H), 2.82 (m, 1 H, 2-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 180.1 (2-C), 100.5 (CH_2, 5-C), 73.4 (CH_2, 3-C), 73.2 (CH_2, 10-C), 70.7 (CH_2, 7-C), 44.0 (CH, 8-C), 43.1 (CH, 2-C), 38.1 (CH, 1-C), 33.8 (CH, 9-C) ppm. IR (ATR): $\tilde{\nu}$ = 2908, 2872, 1745, 1475, 1153, 1015 cm^{-1}. MS: *m*/*z* (%) = 184 (24) [M]$^+$, 154 (10), 85 (100). $C_9H_{12}O_4$ (184.19): calcd. C 58.69, H 6.57; found C 58.72, H 6.47.

Compound 14b: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 4.84 (s, 2 H, 2× 5-H), 4.31 (dd, $^2J_{H,H}$ = 9.6, $^3J_{H,H}$ = 4.9 Hz, 1 H, 10-H), 4.22 (d, $^2J_{H,H}$ = 9.6 Hz, 1 H, 10-H), 4.15 (dd, $^2J_{H,H}$ = 10.9, $^3J_{H,H}$ = 4.7 Hz, 1 H), 4.06 (dd, $^2J_{H,H}$ = 11.1, $^3J_{H,H}$ = 5.5 Hz, 1 H), 3.56 (d, $^2J_{H,H}$ = 11.1 Hz, 1 H), 3.51 (d, $^2J_{H,H}$ = 10.9 Hz, 1 H), 3.20 (m, 1 H, 9-H), 3.08–2.55 (m, 3 H, 1 H, 2-H, 8-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 176.5 (2-C), 92.8 (CH_2, 5-C), 71.9 (CH_2, 3-C), 69.8 (CH_2, 10-C), 67.8 (CH_2, 7-C), 44.8 (CH, 8-C), 40.4 (CH, 2-C), 38.3 (CH, 1-C), 36.7 (CH, 9-C) ppm. MS *m*/*z* (%) = 184 (0.2) [M]$^+$, 154 (0.3), 85 (100).

Compound 15b: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 4.84 (s, 2 H, 2× 5-H), 4.61 (dd, $^2J_{H,H}$ = 10.4, $^3J_{H,H}$ = 6.5 Hz, 1 H, 10-H), 4.54 (d, $^2J_{H,H}$ = 10.4 Hz, 1 H, 10-H), 4.06 (dd, $^2J_{H,H}$ = 11.1, $^3J_{H,H}$ = 5.5 Hz, 1 H), 3.94 (dd, $^2J_{H,H}$ = 11.1, $^3J_{H,H}$ = 5.6 Hz, 1 H), 3.65 (d, $^2J_{H,H}$ = 11.2 Hz, 1 H), 3.60 (d, $^2J_{H,H}$ = 11.1 Hz, 1 H), 3.20 (m, 1 H, 9-H), 3.08–2.55 (m, 3 H, 1-H, 2-H, 8-H) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 176.6 (2-C), 93.1 (CH_2, 5-C), 70.5 (CH_2, 3-C), 68.0 (CH_2, 10-C), 66.5 (CH_2, 7-C), 43.8 (CH, 8-C), 41.1 (CH, 2-C), 38.5 (CH, 1-C), 33.6 (CH, 9-C) ppm. MS *m*/*z* (%) = 184 (0.4) [M]$^+$, 154 (28), 85 (100).

Mixture **14b**–**15b**: $C_9H_{12}O_4$ (184.19): calcd. C 58.69, H 6.57; found C 58.69, H 6.65.

Irradiation of a solution of lactone **10** (150 mg, 1.78 mmol) and (*Z*)-**12** (2.00 g, 16.0 mmol) in acetone (90 mL) through a Pyrex filter for 6 h delivered the unreacted lactone **10** (129 mg, 1.53 mmol) after purification of the crude material by silica gel column chromatography.

(1*R*,2*S*,8*R*,9*S*,10*S*)-10-(Pivaloyloxymethyl)-4,6,11-trioxatricyclo[7.3.0.0^{2,8}]dodecan-12-one (20b), (1*S*,2*R*,8*S*,9*R*,10*S*)-10-(Pivaloyloxymethyl)-4,6,11-trioxatricyclo[7.3.0.0^{2,8}]dodecan-12-one (25b), (1*R*,2*S*,8*S*,9*S*,10*S*)-10-(Pivaloyloxymethyl)-4,6,11-trioxatricyclo[7.3.0.0^{2,8}]dodecan-12-one (19b), and (1*R*,2*R*,8*R*,9*S*,10*S*)-10-(Pivaloyloxymethyl)-4,6,11-trioxatricyclo[7.3.0.0^{2,8}]dodecan-12-one (18b): A solution of **11** (150 mg, 0.76 mmol) and (*Z*)-**12** (894 mg, 6.84 mmol) in acetonitrile (90 mL) was irradiated through a Quartz filter for 4 h. The progress of the reaction was monitored by GC,

where the appearance of four new peaks was observed (54:15:14:17 ratio). Evaporation of the solvent and column chromatography over silica gel (hexane/EtOAc, 10:1 to 1:1) provided the following fractions: (i) a colorless oil identified as **25b** (24 mg, 0.08 mmol, 11% yield), (ii) a white solid identified as **20b** (86 mg, 0.29 mmol, 38% yield), (iii) a 45:55 mixture of **19b** and **18b** (48 mg, 0.16 mmol, 21% yield), and (iv) unreacted starting lactone **11** (10 mg, 0.05 mmol). All the attempts to separate the cycloadducts **19b** and **18b** were unsuccessful and enriched fractions were analyzed.

Compound 20b: M.p. 56–58 °C (EtOAc/pentane). ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 5.19 (d, $^2J_{H,H}$ = 7.4 Hz, 1 H, 5-H), 4.61 (dd, $^3J_{H,H}$ = 3.7, 3.2 Hz, 1 H, 10-H), 4.36 (d, $^2J_{H,H}$ = 7.4 Hz, 1 H, 5-H), 4.24 (dd, $^2J_{H,H}$ = 12.0, $^3J_{H,H}$ = 3.2 Hz, 1 H, CH_2OPiv), 4.17 (dd, $^2J_{H,H}$ = 13.5, $^3J_{H,H}$ = 2.6 Hz, 1 H, 3-H), 4.03 (dd, $^2J_{H,H}$ = 12.0, $^3J_{H,H}$ = 3.7 Hz, 1 H, CH_2OPiv), 3.99 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 3.2 Hz, 1 H, 7-H), 3.78 (dd, $^2J_{H,H}$ = 13.5, $^3J_{H,H}$ = 2.2 Hz, 1 H, 3-H), 3.67 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 1.0 Hz, 1 H, 7-H), 3.21 (dd, $^3J_{H,H}$ = 8.1, 4.9 Hz, 1 H, 9-H), 3.14 (dd, $^3J_{H,H}$ = 8.1, 2.8 Hz, 1 H, 1-H), 2.84 (m, 1 H, 2-H), 2.78 (m, 1 H, 8-H), 1.18 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 179.4 (12-C), 178.0 (C=O, ester), 100.6 (CH_2, 5-C), 82.0 (CH, 10-C), 73.3 (CH_2, 3-C), 70.6 (CH_2, 7-C), 65.6 (CH_2, *C*H_2OPiv), 43.6/43.4 (2× CH, 2-C/8-C), 39.1 (CH, 1-C), 38.8 [$(CH_3)_3C$], 36.1 (CH, 9-C), 27.1 [$(CH_3)_3$C] ppm. IR (ATR): $\tilde{\nu}$ = 2970, 2934, 2868, 1762, 1724, 1479, 1279, 1145, 1085 cm^{-1}. $C_{15}H_{22}O_6$ (298.34): calcd. C 60.39, H 7.43; found C 60.30, H 7.72.

Compound 25b: ^{1}H NMR (250 MHz, $CDCl_3$, 25 °C): δ = 5.20 (d, $^2J_{H,H}$ = 7.2 Hz, 1 H, 5-H), 4.64 (ddd, $^3J_{H,H}$ = 7.3, 6.0, 5.8 Hz, 1 H, 10-H), 4.38 (dd, $^2J_{H,H}$ = 11.8, $^3J_{H,H}$ = 7.3 Hz, 1 H, CH_2OPiv), 4.35 (d, $^2J_{H,H}$ = 7.2 Hz, 1 H, 5-H), 4.21 (dd, $^2J_{H,H}$ = 11.8, $^3J_{H,H}$ = 5.8 Hz, 1 H, CH_2OPiv), 4.18 (dd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 2.9 Hz, 1 H, 3-H), 3.88 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 3.9 Hz, 1 H, 7-H), 3.79 (dd, $^2J_{H,H}$ = 13.3, $^3J_{H,H}$ = 2.8 Hz, 1 H, 3-H), 3.68 (dd, $^2J_{H,H}$ = 13.4, $^3J_{H,H}$ = 1.2 Hz, 1 H, 7-H), 3.52 (dt, $^3J_{H,H}$ = 8.0, 6.0 Hz, 1 H, 9-H), 3.12 (dd, $^3J_{H,H}$ = 8.0, 3.3 Hz, 1 H, 1-H), 2.95 (m, 1 H, 8-H), 2.72 (m, 1 H, 2-H), 1.20 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (62.9 MHz, $CDCl_3$, 25 °C): δ = 179.1 (12-C), 178.0 (C=O, ester), 100.6 (CH_2, 5-C), 78.1 (CH, 10-C), 73.4 (CH_2, 3-C), 70.6 (CH_2, 7-C), 62.3 (CH_2, *C*H_2OPiv), 43.1 (CH, 2-C), 39.7 (CH, 1-C), 38.8 [$(CH_3)_3C$], 37.4 (CH, 8-C), 35.9 (CH, 9-C), 27.1 [$(CH_3)_3$C] ppm. IR (ATR): $\tilde{\nu}$ = 2958, 2941, 2871, 1771, 1729, 1480, 1281, 1147, 1080 cm^{-1}. HRMS (ESI$^+$): calcd. for $C_{15}H_{22}O_6Na$ 321.1309; found 321.1301.

Compound 19b: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 5.01 (ddd, $^3J_{H,H}$ = 5.0, 4.3, 4.2 Hz, 1 H, 10-H), 4.89 (d, $^2J_{H,H}$ = 8.8 Hz, 1 H, 5-H), 4.83 (d, $^2J_{H,H}$ = 8.8 Hz, 1 H, 5-H), 4.16 (m, 1 H, CH_2OPiv), 4.25 (m, 1 H, CH_2OPiv), 4.08 (m, 1 H, 3-H), 3.95 (m, 1 H, 7-H), 3.66 (m, 1 H, 7-H), 3.58 (m, 1 H, 3-H), 3.03 (m, 1 H, 8-H), 2.95 (m, 1 H, 2-H), 2.89 (m, 1 H, 9-H), 2.80 (m, 1 H, 1-H), 1.20 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 178.0 (C=O), 177.9 (C=O), 93.3 (CH_2, 5-C), 76.9 (CH, 10-C), 70.6 (CH_2, 3-C), 66.6 (CH_2, 7-C), 65.1 (CH_2, *C*H_2OPiv), 44.2 (CH, 1-C), 41.2 (CH, 2-C), 39.9 (CH, 8-C), 38.9 [$(CH_3)_3C$], 36.7 (CH, 9-C), 27.1 [$(CH_3)_3$C] ppm. MS *m*/*z* (%) = 298 (0.2) [M]$^+$, 268 (1.2), 197 (0.2), 183 (0.8), 57 (100).

Compound 18b: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 4.83 (s, 2 H, 5-H), 4.57 (dd, $^3J_{H,H}$ = 3.4, 3.0 Hz, 1 H, 10-H), 4.24 (m, 1 H, CH_2OPiv), 4.14 (m, 1 H, 3-H), 4.10 (m, 1 H, CH_2OPiv), 4.06 (m, 1 H, 7-H), 3.54–3.49 (m, 2 H, 3-H, 7-H), 3.26 (m, 1 H, 9-H), 3.00 (m, 1 H, 2-H), 2.83–2.97 (m, 1 H, 1-H), 2.78 (m, 1 H, 8-H), 1.18 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 175.7 (C=O), 175.4 (C=O), 93.0 (CH_2, 5-C), 80.8 (CH, 10-C), 69.8 (CH_2, 3-C), 68.1 (CH_2, 7-C), 65.0 (CH_2, *C*H_2OPiv), 45.0 (CH, 2-C), 41.2 (CH, 1-C), 39.4 (CH, 9-C), 38.9 (CH, 8-C), 38.8 [$(CH_3)_3C$], 27.2 [$(CH_3)_3$C] ppm. MS *m*/*z* (%) = 298 (0.2) [M]$^+$, 268 (0.2), 197 (1.1), 183 (16), 57 (100).

Mixture **18b**–**19b**: HRMS (ESI$^+$): calcd. for $C_{15}H_{22}O_6Na$ 321.1309; found 321.1302.

(1*RS*,5*SR*,6*RS*,7*SR*)-6,7-Bis(hydroxymethyl)-3-oxabicyclo[3.2.0]-heptan-2-one (16c), (1*RS*,5*SR*,6*RS*,7*RS*)-6,7-Bis(hydroxymethyl)-3-oxabicyclo[3.2.0]heptan-2-one (14c), and (1*RS*,5*SR*,6*SR*,7*SR*)-6,7-Bis(hydroxymethyl)-3-oxabicyclo[3.2.0]heptan-2-one (15c): A solution of 2(5*H*)-furanone **10** (150 mg, 1.78 mmol) and (*Z*)-**13** (1.3 mL, 16.0 mmol) in acetonitrile (90 mL) was irradiated through a Quartz filter for 3 h. The progress of the reaction was monitored by TLC (hexane/EtOAc, 1:3). Evaporation of the solvent, followed by kugelrohr distillation of (*Z*)-**13** under reduced pressure and silica gel column chromatography (hexane/EtOAc, 1:1 to EtOAc) rendered a mixture of **16c**, **14c**, and **15c** (46:35:19 ratio; 210 mg, 1.22 mmol, 69% yield) and unreacted lactone **10** (18 mg, 0.21 mmol). Repeated column chromatography (hexane/EtOAc, 2:1 to EtOAc) provided the following fractions: (i) an oil identified as **16c**, and (ii) a mixture of **14c** and **15c**. All attempts to separate the cycloadducts **14c** and **15c** were unsuccessful and enriched fractions were analyzed.

Compound 16c: ^{1}H NMR (250 MHz, [D$_6$]acetone, 25 °C): δ = 4.37 (dd, $^2J_{H,H}$ = 9.3, $^3J_{H,H}$ = 6.3 Hz, 1 H, 4-H), 4.25 (d, $^2J_{H,H}$ = 9.3 Hz, 1 H, 4-H), 3.97–3.63 (m, 4 H, 2× 8-H, 2× 9-H), 2.96 (m, 1 H, 5-H), 2.82 (dd, $^3J_{H,H}$ = 7.8, 2.6 Hz, 1 H, 1-H), 2.66 (m, 1 H, 6-H), 2.63 (m, 1 H, 7-H) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]acetone, 25 °C): δ = 179.4 (2-C), 72.8 (CH_2, 4-C), 60.6, 61.2 (2× CH_2, 8-C, 9-C), 42.7/41.4 (2× CH, 6-C/7-C), 37.7 (CH, 1-C), 36.0 (CH, 5-C) ppm. IR (ATR): $\tilde{\nu}$ = 3600–3000, 2922, 2852, 1752, 1464, 1260, 1167, 1024 cm^{-1}. HRMS (ESI$^+$): calcd. for $C_8H_{12}O_4Na$ 195.0628; found 195.0631.

Compound 14c: ^{1}H NMR (250 MHz, [D$_6$]acetone, 25 °C): δ = 4.36 (dd, $^2J_{H,H}$ = 9.3, $^3J_{H,H}$ = 6.0 Hz, 1 H, 4-H), 4.24 (dd, $^2J_{H,H}$ = 9.3, $^3J_{H,H}$ = 1.3 Hz, 1 H, 4-H), 3.70–3.40 (m, 4 H, 2× 8-H, 2× 9-H), 3.13 (ddd, $^3J_{H,H}$ = 9.3, 7.6, $^4J_{H,H}$ = 1.1 Hz, 1 H, 1-H), 2.90 (m, 1 H, 5-H), 2.59 (m, 1 H, 6-H), 2.27 (m, 1 H, 7-H) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]acetone, 25 °C): δ = 177.9 (2-C), 73.6 (CH_2, 4-C), 64.1/62.7 (2× CH_2, 8-C/9-C), 46.5/39.9 (2× CH, 6-C/7-C), 37.7 (CH, 1-C), 35.0 (CH, 5-C) ppm.

Compound 15c: ^{1}H NMR (250 MHz, [D$_6$]acetone, 25 °C): δ = 4.63 (dd, $^2J_{H,H}$ = 10.0, $^3J_{H,H}$ = 2.3 Hz, 1 H, 4-H), 4.34 (dd, $^2J_{H,H}$ = 10.0, $^3J_{H,H}$ = 8.0 Hz, 1 H, 4-H), 3.70–3.40 (m, 4 H, 2× 8-H, 2× 9-H), 3.20 (dddd, $^3J_{H,H}$ = 10.4, 8.1, 2.3, 1.0 Hz, 1 H, 5-H), 2.90 (m, 1 H, 1-H), 2.59 (m, 1 H, 7-H), 2.59 (m, 1 H, 6-H) ppm. ^{13}C NMR (62.9 MHz, [D$_6$]acetone, 25 °C): δ = 178.6 (2-C), 68.7 (CH_2, 4-C), 64.3/61.7 (2× CH_2, 8-C/9-C), 43.3/38.9 (2× CH, 6-C/7-C), 37.8 (CH, 1-C), 33.0 (CH, 5-C) ppm.

Mixture **14c**–**15c**: IR (ATR): $\tilde{\nu}$ = 3600–3000, 2912, 2873, 1737, 1473, 1373, 1167, 1082 cm^{-1}.

Irradiation of a solution of lactone **10** (150 mg, 1.78 mmol) and (*Z*)-**13** (1.3 mL, 16.0 mmol) in acetone (90 mL) through a Pyrex filter for 4 h delivered a mixture of **16c**, **14c**, and **15c** (43:37:20 ratio; 106 mg, 0.62 mmol, 35% yield) and unreacted lactone **10** (64 mg, 0.76 mmol) after purification of the crude material by silica gel column chromatography.

(1*R*,4*S*,5*S*,6*R*,7*R*)-6,7-Bis(hydroxymethyl)-4-(pivaloyloxymethyl)-3-oxabicyclo[3.2.0]heptan-2-one (18c) and (1*R*,4*S*,5*S*,6*S*,7*S*)-6,7-Bis(hydroxymethyl)-4-(pivaloyloxymethyl)-3-oxabicyclo[3.2.0]-heptan-2-one (19c): A solution of **11** (150 mg, 0.76 mmol) and (*Z*)-

13 (0.56 mL, 6.84 mmol) in acetonitrile (90 mL) was irradiated through a Quartz filter for 4 h. The progress of the reaction was monitored by GC analysis. Evaporation of the solvent, followed by kugelrohr distillation of (*Z*)-**13** under reduced pressure and silica gel column chromatography (hexane/EtOAc, 1:1 to EtOAc), afforded a mixture of **18c**, **19c**, and another unidentified cycloadduct (46:38:16 ratio; 101 mg, 0.35 mmol, 46% yield). By successive column chromatography purifications, fractions enriched in **18c** and **19c** were obtained.

Compound 18c: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 4.64 (dd, $^3J_{H,H}$ = 3.1, 2.5 Hz, 1 H, 4-H), 4.24 (dd, $^2J_{H,H}$ = 12.2, $^3J_{H,H}$ = 2.5 Hz, 1 H, CH_2OPiv), 4.08 (dd, $^2J_{H,H}$ = 12.2, $^3J_{H,H}$ = 3.1 Hz, 1 H, CH_2OPiv), 3.80–3.60 (m, 4 H, 2× 8-H, 2× 9-H), 3.25 (ddd, $^3J_{H,H}$ = 9.2, 7.3, $^4J_{H,H}$ = 1.1 Hz, 1 H, 1-H), 2.64 (m, 1 H, 7-H), 2.70 (dd, $^3J_{H,H}$ = 7.3, 6.4 Hz, 1 H, 5-H), 2.38 (m, 1 H, 6-H), 1.17 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 179.0 (2-C), 178.1 (C=O, ester), 82.4 (CH, 4-C), 65.4 (CH_2, *C*H_2OPiv), 64.0/62.6 (2× CH_2, 8-C/9-C), 44.8 (CH, 6-C), 38.8 $(CH_3)_3C$, 38.7 (2× CH, 1-C, 7-C), 36.7 (CH, 5-C), 27.1 [$(CH_3)_3C$] ppm.

Compound 19c: ^{1}H NMR (360 MHz, $CDCl_3$, 25 °C): δ = 5.00 (dd, $^3J_{H,H}$ = 3.6, 3.1 Hz, 1 H, 4-H), 4.25 (dd, $^2J_{H,H}$ = 12.0, $^3J_{H,H}$ = 3.1 Hz, 1 H, CH_2OPiv), 4.08 (dd, $^2J_{H,H}$ = 12.0, $^3J_{H,H}$ = 3.6 Hz, 1 H, CH_2OPiv), 3.80–3.60 (m, 4 H, 2× 8-H, 2× 9-H), 3.00 (m, 1 H, 5-H), 3.00 (m, 1 H, 1-H), 2.65 (m, 1 H, 6-H), 2.38 (m, 1 H, 7-H), 1.17 [s, 9 H, (*t*Bu)] ppm. ^{13}C NMR (90.6 MHz, $CDCl_3$, 25 °C): δ = 178.0 (C=O, ester), 177.9 (2-C), 77.8 (CH, 4-C), 66.0 (CH_2, *C*H_2OPiv), 64.5/61.8 (2× CH_2, 8-C/9-C), 42.9 (CH, 7-C), 40.2 (CH, 6-C), 38.8 [$(CH_3)_3C$], 38.7 (CH, 1-C), 35.1 (CH, 5-C), 27.1 [$(CH_3)_3C$] ppm.

General Procedure for Photoisomerization of (*E*)- and (*Z*)-1,4-Dichloro-2-butene (5): A solution of (*E*)-**5** or (*Z*)-**5** (2.00 g, 16.0 mmol) in acetonitrile (90 mL) was irradiated through a Quartz or Pyrex filter for 2 h with or without the presence of 2(5*H*)-furanone **10** (150 mg, 1.78 mmol). The *E*/*Z* ratio was monitored by GC analysis.

Methanolysis of a Mixture of 16b, 43b, and 15b: To a solution of a mixture of **16b**, **43b**, and **15b** (30 mg, 0.15 mmol) in MeOH (5 mL), *p*TsOH (15 mg, 0.07 mmol) was added and the mixture was stirred at room temperature for 48 h. The reaction progress was monitored by TLC (EtOAc). After evaporation of the solvent, the residue was purified by silica gel column chromatography, affording a mixture of **16c**, **14c**, and **15c** (70:15:15 ratio; 20 mg, 0.11 mmol, 76% yield).

Methanolysis of a Mixture of 20b, 25b, 19b, and 18b: To a solution of a mixture of **20b**, **25b**, **19b**, and **18** (38 mg, 0.12 mmol) in MeOH (4 mL), *p*TsOH (12 mg, 0.06 mmol) was added and the mixture was stirred at room temperature for 4 h. The reaction progress was monitored by GC. After evaporation of the solvent, the residue was purified by silica gel column chromatography, affording a mixture of **20c**, **25c**, **19c**, and **18c** (54:15:14:17 ratio; 26 mg, 0.08 mmol, 74% yield).

Supporting Information (see footnote on the first page of this article): Copies of NMR spectra of selected compounds.

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