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Studies towards the total synthesis of solanoeclepin A: enantioselective synthesis of the right-hand substructure

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CHAPTER 2

INTRAMOLECULAR [2+2]-PHOTOCYCLOADDITIONS OF 2-(3-ALKENYL)-3-METHYL-2-CYCLOHEXENONES

2.1 Introduction

The highly strained bicyclo[2.1.1]cyclohexane core of solanoeclenpin A (1) is a structural feature which is, as far as we know, unprecedented in natural products. This strained moiety is part of the right-hand side (3) and much research has been devoted in our group to develop a synthetic route towards this substructure (Scheme 2.1).\textsuperscript{1}

![Scheme 2.1](image)

Initial investigations were focused on constructing the bicyclo[2.1.1]cyclohexane framework via a [2+2]-photocycloaddition using 6-methyldioxenones as substrate.\textsuperscript{1a-\textsuperscript{c}} Crucial for the formation of the required regioisomer was the presence of a butenolide. Substrate 7 gave straight adduct 8 upon irradiation, whereas 9 provided crossed cycloadduct 10 accommodating the desired bicyclo[2.1.1]cyclohexane substructure (Scheme 2.2).
A subsequent approach was the highly regioselective intramolecular butenolide allene [2+2]-photocycloaddition, of which an example is shown in Scheme 2.3. Upon irradiation of 11 a smooth cycloaddition was observed affording 12 in 70% yield. Further elaboration of 12 into 13 required nine steps. Of these nine steps, seven were needed for the generation of the secondary hydroxyl group and bridgehead methyl group from the γ-lactone.

We reasoned that we could simply prevent such a laborious procedure by using a photosubstrate such as 14 (Scheme 2.4). This substrate already contains a protected secondary hydroxyl group in the tether and a methyl group on the enone. Both these groups will end up at the correct position upon cycloaddition in a crossed fashion (15).
Consequently, the butenolide chromophore is given up for an enone. However, intramolecular [2+2]-photocycloadditions between 3-methylcyclohexenones and alkenes, connected via a two atom tether at the enone α-carbon, have not been reported in literature. Therefore, in order to test the viability of this new strategy, simple model substrates were investigated first. This should provide insight whether such substrates participate in the intramolecular [2+2]-photocycloaddition and what regioselectivity will be. Depending on the obtained results more elaborate substrates will be studied bearing different substituents (R₁, R₂, OR₃). In turn, this further study should provide insight in the stereoelectronic effects of these substituents on the [2+2]-photocycloaddition and if the tolerated functional groups are suitable for the conversion into either a carbonyl (R₂) or for building up the cyclopropanecarboxylic acid group (R₁)

### 2.2 Cycloadditions of 3-methyl-2-cyclohexenones with acyclic alkenes

Our first objective was to study substrates 17 and 19 (Scheme 2.5). Both compounds were prepared according to a literature procedure from 3-methyl-4-carbethoxy-2-cyclohexene-1-one (16) by alkylation at C-2 with a suitable 3-alkenyl halide and subsequent decarboxylation.²

Irradiating a solution of parent model substrate 17 in a mixture of MeCN/acetone (9:1 v/v) at 300 nm for 2 h resulted in the complete conversion of the starting material according to TLC.
analysis (Scheme 2.5). The purification of the reaction mixture, however, was difficult due to many byproducts. Repeated chromatography eventually led to a pure cycloadduct in 14% yield. The structure of crossed photocycloadduct 18 was established on the NOEs depicted in Scheme 2.5. The bridgehead methine proton (δ = 2.29 ppm) showed a NOE with the two bridgehead protons of the cyclobutane ring (δ = 1.17 ppm and δ = 2.56 ppm). Furthermore, a NOE with the methyl group (δ = 0.84 ppm) was observed which was pivotal for its assignment as crossed cycloadduct 18.

We then turned our attention to substrate 19 which has two methyl groups at terminal position of the tethered alkene (Scheme 2.6). Exposure of 19 to the same irradiation conditions for 4 h resulted in the complete conversion of the starting material. Examination of the crude reaction mixture with 1H NMR revealed, much to our surprise, the presence of two signals at 4.94 ppm and 4.59 ppm as sharp singlets. Purification of the mixture resulted in the isolation of a pure product in 34% yield. Full analysis of this compound with 2D NMR led us to assign structure 20 to it. The relative stereochemistry was determined using NOE difference experiments. The methine proton adjacent to the carbonyl (δ = 2.71 ppm), showed a NOE with the methyl group on the double bond (δ = 1.80 ppm) and an olefinic proton (δ = 4.59 ppm). The proposed mechanism for the formation of 20 will be discussed in section 2.6 of this chapter.

Scheme 2.6.

Because we obtained the bicyclo[2.1.1]hexane framework upon irradiation of 17, we continued our investigation with the introduction of other substituents at C-4 of the 3-alkenyl side chain of 17 by means of cross metathesis. Thus, exposure of 17 to methyl acrylate in the presence of Grubbs’ second generation catalyst in toluene at 70 ºC for 1.5 h resulted in the isolation of desired acrylate 21 in 57% yield as a single isomer (Scheme 2.7). Based on a coupling constant of 15.6 Hz, the E geometry was assigned to 21. Unfortunately, no
photochemical [2+2]-cycloaddition was observed under various conditions and starting material was recovered in all cases.

\[
\begin{align*}
17 & \xrightarrow{\text{methyl acrylate, Grubbs’ 2nd generation catalyst (5 mol%)}, \text{toluene, 70 °C, 1.5 h (57%)}} 21 \\
23 & \xrightarrow{\text{hv (300 nm), MeCN/acetone, (9:1), 1.5 h (89%)}} 24 \\
1. & \text{allyl acetate, Grubbs’ 1st generation catalyst (3 mol%), CH}_2\text{Cl}_2 \text{ reflux, 16 h} \\
2. & \text{K}_2\text{CO}_3, \text{MeOH, rt, 1.5 h (73% over two steps)}
\end{align*}
\]

**Scheme 2.7.**

Although we were disappointed by the inability of 21 to undergo a photochemical [2+2]-cycloaddition, we continued our investigation with the treatment of 17 with Grubbs’ first generation catalyst in the presence of allyl acetate. This resulted in the formation of the desired allylic acetate along with dimers of allyl acetate and dimers of 17, which hampered the purification. Therefore the acetate group was removed by treatment of the crude mixture with K$_2$CO$_3$ in MeOH. In this way allylic alcohol 23 could be isolated in 73% yield over two steps as a mixture of isomers (E/Z ca. 72:28).

Interestingly, after 1.5 h of irradiation of this E/Z-mixture under standard conditions, a single cycloadduct was isolated in 89% yield. To unambiguously assign its structure as crossed cycloadduct 24, the hydroxyl group was subsequently converted into the crystalline p-nitrobenzoate 25 in 76% yield. Recrystallization provided crystals (mp 95–97 °C) suitable for X-ray analysis (Figure 2.1).
Chapter 2

Figure 2.1. Crystal structure of 25.

Intrigued by the pronounced effect induced by the methyl ester and the hydroxymethyl group on the outcome of the [2+2]-photocycloaddition, we decided to synthesize substrates 26 and 27 for further study (see Scheme 2.8 and 2.9). These substrates have their substituent at C-3 of the 3-alkenyl side chain instead of at C-4 as in 21 and 23.

The synthesis of photosubstrates 26 and 27 commenced with alcohol 28 which was prepared in four steps from 1,4-butanediol according to a literature procedure (Scheme 2.8). Silylation of the primary allylic alcohol was followed by cleavage of the benzoate which afforded alcohol 30 in 82% yield. This alcohol was subsequently converted into the corresponding mesylate 31 which proved to be a suitable alkylating agent for the anion of 16. Coupling product 32 was obtained in 69% yield. Decarboxylation and desilylation furnished photosubstrate 26.

Scheme 2.8.
Photosubstrate 27 was obtained directly from 26 according to a procedure of Corey and co-workers. Therefore, allylic alcohol 26 was oxidized to aldehyde 35 using manganese dioxide. Addition of KCN, acetic acid and again manganese dioxide to a methanolic solution of the crude aldehyde 35 resulted in the formation of acrylate 27 in 51% yield (Scheme 2.9).

Unfortunately, the irradiation of 26 under standard conditions resulted in the formation of a complex mixture of products and 34 was not formed in a useful amount. A smooth [2+2]-photocycloaddition was observed, however, upon irradiation of 27 and after 2 h complete conversion was reached according to TLC analysis. Purification led to crystalline cycloadduct 36 in 72% yield.

**Scheme 2.9.**

![Scheme 2.9](image)

**Figure 2.2.** Crystal structure of 36.
Recrystallization from \( n \)-hexane provided crystals (mp 91 °C) suitable for X-ray crystallographic analysis which unambiguously confirmed the formation of the desired crossed cycloadduct (Figure 2.2).

### 2.3 Cycloadditions of 3-methyl-2-cyclohexenones with \( \alpha \)- and \( \beta \)-substituted butenolides

Based on the results obtained so far we reasoned that we could now rationally design a photosubstrate by simply combining 23 and 27, which both provided the crossed cycloadduct in good yield (Figure 2.3). However, instead of preserving the open chain structure we decided to connect the alcohol and ester function to form a butenolide (see 38 Scheme 2.10).

**Figure 2.3.** Substrates which afforded the crossed cycloadduct upon irradiation

We envisioned that 38 should be accessible by the oxidation of furan 37 which was prepared according to a literature procedure.\(^5\) The oxidation of the furan proceeded smoothly providing butenolide 38 in 57% yield over two steps (Scheme 2.10).\(^6\)

**Scheme 2.10.**

Complete conversion of the starting material was observed according to TLC analysis after 1.5 h of irradiation under standard conditions. Purification using flash column chromatography gave a product which was further purified by recrystallization from cyclohexane/diethyl ether. This resulted in the isolation of a pure photoproduct in 50% yield as colorless needles (mp 100 °C).
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

Full analysis of this product using 2D NMR and NOE difference experiments led us to assign structure 39 to it. Most indicative for this assignment was the NOE between the methyl group (δ = 1.28 ppm) and the bridgehead proton (δ = 3.03 ppm). This structural assignment was eventually fully supported by X-ray crystallographic analysis (Figure 2.4).

![Crystal structure of 39](image)

Figure 2.4. Crystal structure of 39

This sudden preference for the straight mode of cyclization put forward the question what the effect on the regioselectivity would be if the tethered enone were connected at the β-carbon of the butenolide (see 41 Scheme 2.11).

Scheme 2.11.
The synthesis of 41 commenced with alcohol 26, which was esterified with acryloyl chloride to give 40 in 65% yield. Slow addition of a solution of Grubbs’ first generation catalyst in CH$_2$Cl$_2$ over a period of 4 h at room temperature was followed by reflux overnight to furnish desired β-substituted butenolide 41 in 69% yield.

The photocycloaddition, however, proved to be a slow reaction and required 18 h under standard irradiation conditions to reach a useful conversion of the starting material. Purification of the complex mixture resulted in the isolation of a pure product in only 5% yield. Full analysis of this product using 2D NMR and NOE difference experiments led us to assign structure 42 to it. The most indicative NOE was observed between the methyl group (δ = 1.50 ppm) and the methine proton adjacent to the lactone carbonyl (δ = 2.95 ppm).

**2.4 Cycloaddition of 3-methyl-2-cyclohexenone bearing a 2-(2-ethylpent-2-enenitrile) side chain**

The exclusive formation of straight cycloadducts from substrates 38 and 41 led us to turn our attention to the synthesis of an open chain analog. After some experimentation an efficient route was found, starting from iodoenone 43, which was prepared from the parent enone by direct α-iodination (scheme 2.12).

Protection of the ketone as an acetal furnished 44 in 97% yield. A Negishi coupling of 44 with commercially available 3-cyanopropylium zinc bromide provided coupling product 45 in 73% yield. Treatment of 45 with LDA at –78 °C in THF was followed by the addition of propanal. We decided to use this aldehyde because we first wanted to investigate the influence of a simple ethyl chain. After acidic workup enone 46 was isolated in 67% yield. Installation of the double bond was accomplished in two steps via mesylation of the hydroxyl group followed by elimination with DBU to give photosubstrate 47 in 54% yield as an $E/Z$ mixture (ca. 60:40).

Substrate 47 was subjected to the regular irradiation conditions for 2 h. Purification led to the isolation of two products. The major product was assigned to be crossed adduct 48. Extensive analysis of the minor product with 2D NMR and NOE difference experiments led us to assign straight structure 49 to it, which was isolated in 31% yield. Most indicative for its assignment was the NOE between the methyl group (δ 1.17 ppm) and the methine proton (δ 2.48 ppm).

Interestingly, this is the first example during this study of a [2+2]-photocycloaddition leading to the formation of both the straight and the crossed cycloadduct.
2.5 Cycloaddition of 3-methyl-2-cyclohexenone bearing a 2-(methyl-(1-oxy)-3-methylenebutenoate) side chain

Having independently investigated the influence of substituents at C-3 and C-4, our next objective was the introduction of an oxygen substituent at C-1 of the 3-alkenyl side chain. A straightforward approach towards γ-hydroxyester 51 would be the addition of aldehyde 50 to the lithium derivative of 44 (Scheme 2.13).10

Scheme 2.13.

However, addition of 50 to the lithium derivative of 44 did not furnish coupling product 51. Interestingly, Snapper and co-workers reported the coupling of aldehydes bearing α-protons with the lithium derivative of acetal protected α-bromocyclohexenone, which proceeded in good...
yield. Unfortunately, the addition of HMPA or anhydrous CeCl₃ to the lithium derivative of 44 prior to the addition of 50 did not result in the formation of 51. Apparently the reaction failed due to competitive deprotonation of 50 by the organometallic intermediate under the reaction conditions.

Experimental support for this hypothesis was obtained by using unsaturated analog 52, which gave coupling product 53 in 64% yield (Scheme 2.14). Protection of the resulting alcohol as a TBS ether was followed by regioselective hydrogenation of the acrylate which afforded 55 in 98% yield. Interesting to note is the requirement of n-BuNH₂ which was added to prevent cleavage of the acetal group.¹³

The next task was to introduce a methylene substituent next to the ester. This would allow direct comparison with 27, which is lacking a C-1 oxygen substituent at the 3-alkenyl side chain. All attempts to introduce a methylene group using Eschenmoser’s salt¹⁴ proved to be fruitless and gave rise to complex mixtures. This prompted us to employ a different approach which commenced with the treatment of 55 with LDA followed by addition of methyl formate. The desired formylated product was isolated as a mixture of isomers (56). Conversion of 56 into the corresponding enol triflate was followed by a palladium-catalyzed reduction using triethylsilane as the reductant which eventually gave 57 in 62% over two steps.¹⁵ Hydrolysis of the acetal group under carefully controlled conditions in order to prevent cleavage of the TBS ether completed the synthesis of photosubstrate 58.

Irradiation of a solution of 58 for 2 h resulted in the complete consumption of the starting material. Examination of the crude reaction mixture with ¹H NMR showed the presence of several products of which some contained an aldehyde group. Such products are presumably formed via a [2+2]-photocycloaddition/retro-aldol fragmentation sequence. In turn, this fragmentation is probably caused by cleavage of the TBS group which is apparently not stable. Purification of the mixture resulted in the isolation of a single photocycloadduct in 28% yield. Complete analysis of the product using 2D NMR and NOE difference experiments eventually led us to assign structure 59 to it. The NOE between the proton adjacent to the OTBS ether (δ = 4.55 ppm) and the proton on the cyclobutane (δ = 1.36 ppm) was most indicative for this assignment. Furthermore, this NOE also allowed us to determine that the bridgehead methyl group and the TBS ether had a cis-relationship, which is the correct spatial orientation for the natural product (60).
Cycloadduct 59 is formed when it proceeds through a transition state conformation similar to 58a (Scheme 2.15). In conformation 58a the OTBS group has minimal steric interaction with the methyl group and the carbonyl. A detailed study by Snapper and co-workers, investigating the photocycloaddition of cyclohexenones and cyclopentenones bearing a 2-(1-oxo-alkenyl) side chain, showed that protection of the hydroxyl group is essential for the formation of a single diastereoisomer. 11 Substrates containing a free hydroxyl group gave mixtures of diastereoisomers being epimeric at the carbon bearing the secondary hydroxyl group.
If the behavior observed by Snapper is also true for substrate 58, it would mean that the irradiation of unprotected analog 60 should also lead to the formation undesired diastereoisomer 61. This change in selectivity is caused by the free hydroxyl group which forms an intramolecular hydrogen-bond with the carbonyl group (60a). Consequently this results in a different conformation with respect to 58a. Upon cycloaddition the methyl group and hydroxyl group would be positioned \textit{trans} with respect to each other. Further studies are currently ongoing to verify this hypothesis.

\textbf{2.6 Mechanistic considerations}

The results obtained from this study are summarized in Table 2.1. The majority of the investigated photosubstrates showed ‘normal’ cyclization behaviour according to the "rule of five" and provided the corresponding crossed cycloadducts. However, there are two possible modes of 1,5-closure (see pathway b or c Scheme 2.16). In order to explain the observed substituent effects on the photocycloaddition we propose that either pathway b or c is followed.
### Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

Table 2.1. Overview of the photocycloaddition results

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Cycloadduct</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17 R = H</td>
<td>18 R = H (14%)</td>
</tr>
<tr>
<td>2</td>
<td>21 R = CO₂Me</td>
<td>22 R = CO₂Me (no reaction)</td>
</tr>
<tr>
<td>3</td>
<td>23 R = CH₂OH</td>
<td>24 R = CH₂OH (89%)</td>
</tr>
<tr>
<td></td>
<td>(E/Z 72:28)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>19</td>
<td>20 (34%)</td>
</tr>
<tr>
<td>5</td>
<td>47 (E/Z 60:40)</td>
<td>48 (56%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>49 (31%)</td>
</tr>
<tr>
<td>6</td>
<td>26 R = CH₂OH</td>
<td>34 R = CH₂OH (n.d.)</td>
</tr>
<tr>
<td>7</td>
<td>27 R = CO₂Me</td>
<td>36 R = CO₂Me (72%)</td>
</tr>
<tr>
<td>8</td>
<td>58</td>
<td>59 (28%)</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>39 (50%)</td>
</tr>
<tr>
<td>10</td>
<td>41</td>
<td>42 (&lt;5%)</td>
</tr>
</tbody>
</table>

39
Looking at the cycloadditions of 23 and 47 (entries 3 and 5, Table 2.1), which are both completely stereoconvergent, it is most likely that the formation of 24 and 48 proceeds through pathway b (Scheme 2.16). Because the newly generated radical in intermediate 65 ends up outside the cyclopentane ring the embedded stereochemical information of the alkene is therefore lost. The formation of a single isomer can be rationalized by examining a three-dimensional representation of 65 (Scheme 2.17). As a second carbon-carbon bond is not formed due to steric interactions between the pseudoaxial hydrogen’s and the R² group in 65a, rotation about the former carbon-carbon double bond takes place leading to 65b. Once arrived at this conformation cyclobutane formation can take place. This isomer is formed according to the crystal structure of 25 (see Figure 2.1). By analogy the stereochemistry of 48 was determined.
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

Scheme 2.17.

The formation of the isopropenyl group in 20 can also be explained according to pathway b (Scheme 2.16). Initial formation of intermediate 1,4-biradical 68 from 19, is followed by a hydrogen atom transfer. This process is proposed to be energetically more favorable than carbon-carbon bond formation between two tertiary radicals (Scheme 2.18). 6b,16

Scheme 2.18.

In contrast, upon irradiation of 21 no photocycloaddition was observed (Scheme 2.19). It is reasonable to assume that intermediate 1,4-biradical 69 is formed, because the radicals in 69 are both stabilized by the adjacent electron withdrawing group. Apparently these electrophilic radicals do not form a second carbon-carbon bond. Consequently intermediate 69 reverts to the starting material.

Scheme 2.19.
The substrates containing a methylene substituent (i.e. 17 entry 1, 26 entry 6, 27 entry 7 and 58 entry 8 Table 2.1) are presumed to follow pathway c (Scheme 2.16). This mode of 1,5-closure is presumably favored over pathway b, because it avoids the formation of a primary radical (intermediate 65 \( R^2 = H \), Scheme 2.16). Furthermore, the newly generated radical in 1,4-biradical intermediate 66 ends up adjacent to either an ester group or a hydroxymethyl group. Consequently, these radicals have different electronic properties which, in turn, should influence the outcome of the photocycloaddition. This is what we observe, as 26 (hydroxymethyl group) gives a complex mixture upon irradiation and 27 and 58 (both a methyl ester group) give a smooth cycloaddition.

Scheme 2.20.

The exceptions are substrates 38 and 41 (entry 9 and 10, Table 2.1) which gave the corresponding straight adducts 39 and 42. These products are presumably formed according pathway a (Scheme 2.16). The preference for this pathway is most probably governed by conformational constraints.

Scheme 2.21.

For example, upon 1,5-closure of 38 intermediate 71 is most likely to be formed initially (Scheme 2.21). Intermediate 71, however, does not undergo a second ring closure. A close
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

inspection of the crystal structure of 25 (Figure 2.1) shows the preference for a cis-relationship between the benzoyloxymethyl group and the methyl group on the cyclobutane ring. By analogy this would mean that the cyclobutane ring and the $\gamma$-lactone in 72 have to be forced into a highly unfavourable trans-fusion. An energetically more favourable pathway would therefore be pathway a (Scheme 2.16) leading to the straight cycloadducts 39 and 42 respectively.

2.7 Conclusions

In this chapter our efforts towards an efficient synthesis of the fully substituted bicyclo[2.1.1]hexane core of solanoeclepin A by means of an intramolecular [2+2]-photocycloaddition of 2-(3-alkenyl)-3-methyl-2-cyclohexenones are described. By varying the substitution pattern of the 3-alkenyl side chain we obtained insight in the effect of substituents on the outcome of the [2+2]-photocycloaddition. A methyl ester group at the C-3-position (27 and 58) or a hydroxymethyl group at the C-4-position (23) of the 3-alkenyl side chain seemed to have a positive effect. Interestingly, interconverting the positions of these substituents (21 and 26) on the side chain had a clear negative effect on the cycloaddition, as no product was formed. Furthermore, connecting both substituents in the form of a butenolide (38 and 41) resulted in a sudden preference for the formation of the straight cycloadduct. These results suggest that the fully substituted photosubstrate which is eventually required should not have its substituents at C3 and C4 connected in a cyclic form. This was supported by the irradiation of disubstituted substrate 47, which gave predominantly the desired crossed cycloadduct.

Also an OTBS substituent at C-1 of the 3-alkenyl side chain (58) is tolerated in the [2+2]-photocycloaddition. Upon cycloaddition a preference for the formation of the correct diastereoisomer for the natural product was observed. This preference is presumably governed by the oxygen substituent which forces the substrate to adopt a certain conformation which eventually determines the diastereoselectivity of the photocycloaddition. It is therefore likely that once the chemistry is secured for the synthesis of a fully substituted photosubstrate, bearing an oxygen substituent at C-1, a methyl ester group at C3 and a suitable protected hydroxymethyl group at C-4 of the 3-alkenyl side chain, it would lead to the formation of the fully substituted bicyclo[2.1.1]hexane framework with the correct relative stereochemistry.
2.8 Acknowledgements

Guido Janssen is acknowledged for the synthesis of cycloadducts 26 and 27. Sander Kuijer is thanked for the synthesis of 25. Dennis Schuitemaker is kindly thanked for his work on the synthesis of compounds 21, 23 and 38. Pieter van Delft is kindly acknowledged for his contribution by synthesizing cycloadduct 59. Mathieu André is thanked for the synthesis of compounds 20 and 41. Prenish Bansie is thanked for conducting the preliminary investigations by synthesizing cycloadduct 18 which formed the basis for further study. Dr. René de Gelder and Jan M. M. Smits (Radboud Universiteit, Nijmegen) are kindly acknowledged for crystal structure determinations of cycloadducts 25, 36 and 39. Jan A. J. Geenevasen is acknowledged for his generous help to analyze many NMR spectra. J. W. H. Peeters is thanked for the accurate mass determinations.

2.9 Experimental section

General Information: All reactions involving oxygen or moisture sensitive compounds were carried out under a dry nitrogen atmosphere. THF was distilled from sodium/benzophenone and CH₂Cl₂ and acetonitrile were distilled from CaH₂. The acetone used for the irradiation experiments was of spectrophotometric grade. All commercially available chemicals were used as received. NMR spectra were recorded on a Bruker ARX 400 operating at 400 and 100 MHz for ¹H and ¹³C. Unless otherwise stated, CDCl₃ was used as solvent. Chemical shifts are given in ppm (δ) and were referred to internal solvent signals. IR spectra were measured using a Bruker IFS 28 FT-spectrometer and wavelengths (ν) are reported in cm⁻¹. Mass spectra and accurate mass determinations were performed on a JEOL JMX SX/SX102A, coupled to a JEOL MS-MP7000 data system. The photoreactions were carried out in a quartz reaction vessel with a Rayonet RPR 300 nm. Elemental analyses were performed by Dornis & Kolbe microanalytisches Laboratorium, Mülheim an der Ruhr, Germany.

General procedure for the [2+2]-photocycloadditions: A solution of photosubstrate in a mixture of MeCN/acetone (9:1) was degassed by bubbling argon through the solution for 30 min. The solution was kept under argon atmosphere during the irradiation for the indicated time until complete conversion of the starting material was observed with TLC. The solvent was removed in vacuo and the residue purified.
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

Irradiation of photosubstrate 17 A solution of 17 (100 mg, 0.61 mmol) in a mixture of MeCN/acetonitrile (9:1, 30 mL) was irradiated for 2 h. The reaction mixture was concentrated in vacuo and the residue was purified several times by chromatography (petroleum ether 40–60/EtOAc 9:1) to eventually give 18 (14 mg, 14%) as a colorless oil. \( R_f = 0.3 \) (petroleum ether 40–60/EtOAc 9:1); \(^1\)H NMR: \( \delta 2.58–2.54 \) (m, 1 H), 2.50 (dd, \( J = 14.4, 5.8 \) Hz, 1 H), 2.38 (dt, \( J = 13.5, 3.5 \) Hz, 1 H), 2.32–2.31 (m, 1 H), 2.29–2.24 (m, 1 H), 2.09–2.04 (m, 1 H), 1.91 (dt, \( J = 13.9, 3.9 \) Hz, 1 H), 1.84–1.65 (m, 4 H), 1.62–1.57 (m, 1 H), 1.17 (d, \( J = 7.4 \) Hz, 1 H), 0.85 (s, 3 H); \(^{13}\)C NMR: \( \delta 211.1, 59.4, 51.9, 43.7, 41.0, 39.7, 30.1, 25.3, 24.8, 23.3, 17.7 \).

Irradiation of photosubstrate 19 A solution of 19 (100 mg, 0.52 mmol) in a mixture of MeCN/acetonitrile (9:1, 100 mL) was irradiated for 4 h at 300 nm. The reaction mixture was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc 9:1) to give 20 (34 mg, 0.17 mmol, 34%) as a colorless oil. IR (neat): \( \nu 1713, 1640 \) cm\(^{-1} \); \(^1\)H NMR: \( \delta 4.94 \) (s, 1 H), 4.59 (s, 1 H), 2.71 (dd, \( J = 10.9, 6.9 \) Hz, 1 H), 2.35 (d, \( J = 8.4 \) Hz, 1 H), 2.24 (dd, \( J = 14.0, 5.6 \) Hz, 1 H), 2.19–2.15 (m, 1 H), 2.02–1.95 (m, 2 H), 1.93–1.71 (m, 2 H), 1.77 (s, 3 H), 1.68–1.58 (m, 4 H), 0.82 (s, 3 H); \(^{13}\)C NMR: \( \delta 212.9, 149.1, 110.9, 56.4, 56.2, 51.2, 40.8, 38.4, 27.5, 25.7, 23.8, 21.1, 20.5 \); HRMS (FAB) calculated for C\(_{13}\)H\(_{21}\)O \([\text{MH}^+]\): 193.1592, found: 193.1592.

\((E)\)-Methyl 5-(2-methyl-6-oxocyclohex-1-en-1-yl)pent-2-enoate (21). A solution of 17 (600 mg, 3.65 mmol) in toluene (60 mL) was degassed by bubbling argon through for 40 min. Then methyl acrylate (5.47 mL, 60.8 mmol, 16.7 equiv) was added followed by Grubbs’ second generation catalyst (156 mg, 0.18 mmol, 5%). The mixture was kept under argon and warmed to 70 °C. After 1.5 h the mixture was concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 4:1) to give 21 (462 mg, 57%) as a yellow oil. \( R_f = 0.3 \) (petroleum ether 40–60/EtOAc 4:1); IR (neat): \( \nu 2948, 1719, 1656, 1627 \) cm\(^{-1} \); \(^1\)H NMR: \( \delta 6.77 \) (dt, \( J = 15.6, 7.1 \) Hz, 1 H), 5.62 (d, \( J = 15.6 \) Hz, 1 H), 3.53 (s, 3 H), 2.26 (t, \( J = 7.3 \) Hz, 2 H), 2.12 (t, \( J = 6.5 \) Hz, 4 H), 2.05 (q, \( J = 7.1 \) Hz, 2 H), 1.19–1.72 (m, 5 H); \(^{13}\)C MR: \( \delta 197.7, 166.4, 155.8, 148.4, 134.6, 121.1, 20.5 \).
2-(5-hydroxypent-3-en-1-yl)-3-methylcyclohex-2-enone (23)

To a solution of 17 (500 mg, 3.0 mmol) in CH$_2$Cl$_2$ (70 mL) under argon was added allyl acetate (644 mg, 6.0 mmol, 2 equiv) and Grubbs’ first generation catalyst (75 mg, 0.09 mmol, 3%). The mixture was kept under argon and warmed to reflux. After 16 h the mixture cooled to room temperature and concentrated in vacuo. The residue was dissolved in a mixture of PE/EtOAc (4:1) and filtered over a short path of silica gel. The filtrate was concentrated in vacuo and the residue dissolved in dry MeOH (25 mL). To the solution was added K$_2$CO$_3$ (2.6 g, 19.2 mmol, 6.4 equiv) and the mixture was stirred at room temperature for 1.5 h. After the addition of water (20 mL) the mixture was extracted with CH$_2$Cl$_2$ (3 × 30 mL) and the combined organic layers were dried over MgSO$_4$. The mixture was concentrated in vacuo and the residue was purified by chromatography (petroleum ether 40–60/EtOAc 6:4) to give 23 (425 mg, 73 %) as a yellow oil. $R_f$ = 0.3 (petroleum ether 40–60/EtOAc 6:4); IR (neat): 3416, 2926, 1653, 1624 cm$^{-1}$; $^1$H NMR: $\delta$ 5.62–5.42 (m, 2 H), 4.05 (d, $J$ = 6.4 Hz, 0.56 H, Z isomer), 3.96 (d, $J$ = 5.4 Hz, 1.44 H, E isomer), 2.97 (br s, 1 H), 2.29–2.23 (m, 6 H), 2.03–1.93 (m, 2 H), 1.92–1.82 (m, 5 H); $^{13}$C NMR (of the E isomer): $\delta$ 198.8, 156.4, 134.6, 131.8, 129.2, 62.9, 37.5, 32.5, 31.3, 24.5, 21.9, 21.1; HRMS (FAB) calculated for C$_{12}$H$_{19}$O$_2$ [MH$^+$]: 195.1385, found: 195.1388.

Irradiation of photosubstrate 23 A solution of 23 (120 mg, 0.62 mmol) in a mixture of MeCN/acetone (9:1, 30 mL) was irradiated for 1.5 h at 300 nm. The mixture was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc 1:1) to give 24 (107 mg, 89%) as a colorless oil. $R_f$ = 0.27 (petroleum ether 40–60/EtOAc 1:1); IR (neat): ν 3404, 2946, 1691 cm$^{-1}$; $^1$H NMR: $\delta$ 3.50–3.40 (m, 2 H), 2.99 (t, $J$ = 6.8 Hz, 1 H), 2.58 (dt, $J$ = 14.6, 5.8 Hz, 1 H), 2.45 (dt, $J$ = 14.0, 3.9 Hz, 1 H), 2.27–2.25 (m, 2 H), 2.09–2.05 (m, 1 H), 1.94–1.85 (m, 2 H), 1.76–1.53 (m, 5 H), 0.87 (s, 3 H); $^{13}$C NMR: $\delta$ 211.1, 60.3, 59.2, 50.3, 49.4, 44.6, 39.4, 29.0, 24.7, 22.3, 20.0, 16.8; HRMS (FAB) calculated for C$_{12}$H$_{19}$O$_2$ [MH$^+$]: 195.1385, found: 195.1385.
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

**Synthesis of 25.** To a solution of 24 (124 mg, 0.64 mmol) in CH₂Cl₂ (5 mL) was added pyridine (1.5 mL, 1.91 mmol, 1.9 equiv) followed by p-nitrobenzoyl chloride (356 mg, 1.91 mmol, 1.9 equiv) and the mixture was stirred at room temperature for 18 h. After the addition of water (10 mL) the layers were separated and the aqueous layer was extracted with CH₂Cl₂ (4 × 50 mL). The combined organic layers were dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 8:2) to give 25 (165 mg, 76%) as a crystalline solid, mp 95–97 °C; R₇ 0.2 (petroleum ether 40–60/EtOAc 8:2); IR (neat): ν 2960, 1724, 1697, 1525, 1274 cm⁻¹; ¹H NMR: δ 8.28 (d, J = 8.9 Hz, 2 H), 8.09 (d, J = 8.9 Hz, 2 H), 4.33 (dd, J = 11.5, 5.8 Hz, 1 H), 4.11 (dd, J = 11.5, 8.9 Hz, 1 H), 3.27–3.24 (m, 1 H), 2.56–2.42 (m, 3 H), 2.39–2.38 (m, 1 H), 2.31–2.27 (m, 1 H), 2.13–2.08 (m, 1 H), 1.98–1.61 (m, 5 H), 0.94 (s, 3 H); ¹³C NMR: δ 209.6, 164, 150.4, 135.1, 130.5, 123.4, 62.5, 60.4, 50.7, 45.4, 44.9, 39.2, 28.9, 24.6, 22.2, 19.8, 16.8; HRMS (EI) calculated for C₁₉H₂₁NO₅: 343.1420, found: 343.1420. Recrystallization from PE/EtOAc afforded crystals suitable for X-ray analysis (see Table 2.2 for the crystal structure data).

3-(((Triisopropylsilyl)oxy)methyl)but-3-en-1-yl benzoate (29) To a solution of alcohol 28³ (21.6 g, 0.1 mol) in DMF (500 mL) was added imidazole (16.4 g, 0.24 mol, 2.4 equiv) followed by TIPSCl (27 mL, 0.13 mol, 1.3 equiv) and stirred at room temperature for 18 h. The mixture was poured into water and extracted with diethyl ether (5 × 100 mL). The combined organic layers were washed with water (4 × 100 mL), dried over MgSO₄ and concentration in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 15:1) to give 29 (26.67 g, 70 %) as a colorless oil. R₇ = 0.4 (petroleum ether 40–60/EtOAc 15:1); IR (neat): ν 2950, 2863, 1722, 1460, 1383, 1273, 1114, 1064, 882 cm⁻¹; ¹H NMR: δ 8.05 (d, J = 7.0 Hz, 2 H), 7.55 (t, J = 7.4 Hz, 1 H), 7.46–7.42 (t, J = 7.8 Hz, 2 H), 5.22 (s, 1 H), 4.99 (s, 1 H), 4.47 (t, J = 6.8 Hz, 2 H), 4.26 (s, 2 H), 2.53 (t, J = 6.7 Hz, 2 H), 1.16–1.05 (m, 21 H); ¹³C NMR: δ 166.4, 144.6, 132.7, 130.2, 129.4, 128.2, 110.6, 65.9, 63.4, 31.9, 17.8, 11.8; HRMS (FAB) calculated for C₂₁H₃₅O₃Si [MH⁺]: 363.2355, found: 363.2343.
3-((Triisopropylsilyloxy)methyl)but-3-en-1-ol (30) To a solution of 29 (26.67 g, 73.6 mmol) in MeOH (470 mL) was added K₂CO₃ (40.7 g, 0.29 mol, 4 equiv) and the mixture was stirred at room temperature for 1.5 h. The reaction was quenched by adding brine (500 mL) and the mixture was extracted with EtOAc (3 × 150 mL). The combined organic layers were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 4:1) to give 30 (15.6 g, 82%) as a colorless oil. \( R_f = 0.28 \) (petroleum ether 40–60/EtOAc 4:1); IR (neat): \( \nu = 3339, 2942, 2866, 1462, 1115, 1065, 1047, 881, 808, 681, 668 \) cm⁻¹; \(^1\)H NMR: \( \delta = 5.18 \) (s, 1 H), 4.96 (s, 1 H), 4.20 (s, 2 H), 3.74 (t, \( J = 5.9 \) Hz, 2 H), 2.82 (br s, 1 H), 2.36 (t, \( J = 6.0 \) Hz, 2 H), 1.20–1.05 (m, 21 H); \(^{13}\)C NMR: \( \delta = 145.4, 111.9, 66.3, 61.1, 36.6, 17.7, 11.8 \); HRMS (FAB) calculated for \( \text{C}_{14}\text{H}_{31}\text{O}_{2}\text{Si} \) [MH⁺]: 259.2093, found: 259.2091.

3-(Hydroxymethyl)but-3-enyl methanesulfonate (31) A solution of 30 (15.6 g, 60.4 mmol) in CH₂Cl₂ (400 mL) was cooled to 0 °C followed by the addition of MsCl (5.61 mL, 72.5 mmol, 1.2 equiv). The mixture was left to stir for 15 min and Et₃N (12.63 mL, 90.6 mmol, 1.5 equiv) was added dropwise. Stirring was continued for 1 h at 0 °C and the reaction was quenched by the addition of water (200 mL). The aqueous layer was extracted with CH₂Cl₂ (2 × 100 mL) and the combined organic layers were dried over MgSO₄ and concentrated in vacuo to give crude mesylate 31 (20.42 g). IR (neat): \( \nu = 2941, 2866, 1464, 1352, 1173, 1117, 1067, 955, 905, 881, 806, 681, 660 \) cm⁻¹; \(^1\)H NMR: \( \delta = 5.20 \) (s, 1 H), 4.95 (s, 1 H), 4.36 (t, \( J = 6.9 \) Hz, 2 H), 4.19 (s, 2 H), 3.00 (s, 3 H), 2.52 (t, \( J = 6.9 \) Hz, 2 H), 1.16–1.04 (m, 21 H); \(^{13}\)C NMR: \( \delta = 143.2, 111.8, 68.2, 66.0, 37.3, 32.3, 17.8, 11.8 \).

Coupling product 32 To a suspension of NaH (60 wt. % dispersion of mineral oil, 2.44 g, 61 mmol, 1.01 equiv) in THF (40 mL) was added 3-methyl-4-carbethoxy-2-cyclohexene-1-one (16) (10.5 mL, 60.4 mmol, 1 equiv) at 0 °C. The mixture was warmed to reflux and stirred for 5 h and cooled again to 0 °C. A solution of mesylate 31 (20.42 g) in THF (10 mL) was slowly added. The mixture was warmed to reflux and stirred overnight. Then the mixture was allowed to cool to room temperature and quenched by the addition of saturated aqueous NH₄Cl (50 mL). The mixture was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried over
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 5:1) to give 32 (17.7 g, 69%) as an orange oil. Rᵢ = 0.35 (petroleum ether 40–60/EtOAc 5:1); IR (neat): v: 2941, 2866, 1732, 1670, 1379, 1155, 1111, 881, 808, 681, 668 cm⁻¹; ¹H NMR: δ 5.10 (s, 1 H), 4.85 (s, 1 H), 4.22–4.18 (m, 4 H), 3.29 (t, J = 4.9 Hz, 1 H), 2.62–2.53 (m, 1 H), 2.48 (t, J = 7.9 Hz, 2 H), 2.37 (dt, J = 16.9, 5.2 Hz, 1 H), 2.29–2.15 (m, 2 H), 2.03–2.00 (m, 5 H), 1.28 (t, J = 7.1 Hz, 3 H), 1.15–1.05 (m, 21 H); ¹³C NMR: δ 197.0, 172.0, 150.0, 148.1, 137.1, 108.3, 65.6, 61.0, 47.5, 34.5, 31.4, 25.4, 23.9, 20.2, 17.9, 14.0, 11.8. HRMS (FAB) calculated for C₂₅H₄₃O₄Si [MH⁺]: 423.2931, found: 423.2927.

3-Methyl-2-(3-((triisopropylsilyloxy)methyl)but-3-enyl)cyclohex-2-enone (33) Keto ester 32 (17.7 g, 41.8 mmol) was dissolved in 40 mL of a solution of 15% KOH in EtOH. The mixture was warmed to reflux and stirred for 3.5 h. Then the mixture was allowed to cool to room temperature and quenched by the careful addition of saturated aqueous NH₄Cl. Water (100 mL) was added and the mixture was extracted with CH₂Cl₂ (4 × 50 mL). The combined organic layers were dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 4:1) to give 33 (5.04 g, 34%) as a yellow oil. Rᵢ = 0.45 (petroleum ether 40–60/EtOAc 4:1); IR (neat): v: 2942, 2864, 1664, 1458, 1379, 1111, 1067, 881, 810, 679, 658 cm⁻¹; ¹H NMR: δ 5.12 (s, 1 H), 4.86 (s, 1 H), 4.19 (s, 2 H), 2.45 (t, J = 7.9 Hz, 2 H), 2.40–2.33 (m, 4 H), 1.99 (t, J = 8.6 Hz, 2 H), 1.96–1.92 (m, 5 H), 1.17–1.07 (m, 21 H); ¹³C NMR: δ 198.4, 155.4, 143.4, 135.2, 108.0, 65.7, 37.7, 32.7, 31.7, 23.9, 22.1, 21.0, 17.9, 11.9; HRMS (FAB) calculated for C₂₄H₄₅O₄Si [MH⁺]: 423.2931, found: 423.2927.

2-(3-(hydroxymethyl)but-3-enyl)-3-methylcyclohex-2-enone (26) To a solution of 33 (5.04 g, 14.4 mmol) in THF (350 mL) was added TBAF (1.0 M in THF, 15.84 mL, 15.84 mmol 1.1 equiv). The reaction mixture was stirred at room temperature for 30 min and quenched by the addition of saturated aqueous NH₄Cl (100 mL). The aqueous layer was extracted with EtOAc (3 × 100 mL) and the combined organic layers were washed with brine (100 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 1:2) to give 26 (2.14 g, 77%) as a colorless oil. Rᵢ = 0.39 (petroleum ether 40–60/EtOAc 1:2); IR (neat): v
3377, 2924, 2868, 1647, 1456, 1429, 1379, 1180, 1049, 1030, 893 \text{ cm}^{-1}; \text{^1H NMR:}\delta 4.94 (s, 1 H), 4.77 (s, 1 H), 4.08 (s, 2 H), 2.93 (br s, 1 H), 2.41 (t, J = 7.4 Hz, 2 H), 2.35–2.31 (m, 4 H), 2.02 (t, J = 8.0 Hz, 2 H), 1.91–1.86 (m, 5 H); \text{^13C NMR:}\delta 199.2, 156.3, 148.6, 134.8, 109.6, 65.7, 37.6, 32.7, 32.2, 23.7, 22.0, 21.0; \text{HRMS (FAB) calculated for C}_{12}H_{19}O_{2} [MH]^+: 195.1385, found: 195.1388.

**Methyl 4-(2-methyl-6-oxocyclohex-1-en-1-yl)-2-methylene butanoate**

(27) To a solution of alcohol 26 (250 mg, 1.3 mmol) in hexane/CH$_2$Cl$_2$ (9:1, 36 mL) was added MnO$_2$ (2.35 g, 27 mmol, 25 equiv). The resulting suspension was stirred for 2 h at room temperature followed by filtration over Celite. Removal of the solvent gave the crude aldehyde 35 (230 mg, ca. 95%) which was dissolved in MeOH (40 mL). To this solution was added KCN (440 mg, 6.8 mmol, 6.2 equiv), acetic acid (130 mg, 2.1 mmol, 1.9 equiv) and activated MnO$_2$ (2.35 g, 27 mmol, 25 equiv). This suspension was stirred overnight at room temperature followed by filtration over Celite. The mixture was concentrated in vacuo and the residue was dissolved in EtOAc (25 mL) and washed with water (25 mL), brine (25 mL), dried over MgSO$_4$ and concentrated in vacuo. The residue was purified by column chromatography (petroleum ether 40–60/EtOAc 3:1) to give 27 (120 mg, 51%) as a slightly yellow oil. $R_f = 0.3$ (petroleum ether 40–60/EtOAc 3:1); IR (neat): ν 2948, 1720, 1661, 1628 cm$^{-1}$; \text{^1H NMR:}\delta 6.14 (d, J = 1.4 Hz, 1 H), 5.57 (q, 1.2 Hz, 1 H), 3.78 (s, 3 H), 2.48 (t, J = 7.1 Hz, 2 H), 2.41–2.31 (m, 6 H), 1.97–1.92 (m, 5 H); \text{^13C NMR:}\delta 198.4, 167.4, 156.2, 139.9, 134.3, 125.1, 51.5, 37.6, 32.6, 31.1, 30.0, 24.2, 22.0, 20.9; \text{HRMS (FAB) calculated for C}_{13}H_{19}O_{3} [MH]^+: 223.1334, found: 223.1330.

**Irradiation of photo-substrate 27** A solution of 27 (100 mg, 0.45 mmol) in a mixture of MeCN/acetone (9:1, 30 mL) was irradiated for 2 h at 300 nm. The mixture was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc 3:1) to give 36 (72 mg, 72%) as a solid, mp 91 °C; $R_f = 0.28$ (petroleum ether 40–60/EtOAc 3:1); IR (neat): ν 2950, 1728, 1698 cm$^{-1}$; \text{^1H NMR:}\delta 3.72 (s, 3 H), 2.81 (dt, J = 7.6, 2.9 Hz, 1 H), 2.48 (td, 14.7, 5.8 Hz, 1 H), 2.33 (14.2, 3.6 Hz, 1 H), 2.31–2.27 (m, 1 H), 2.09–1.79 (m, 6 H), 1.62 (d, J = 13.3 Hz, 1 H), 1.55 (d, J = 7.6 Hz, 1 H), 1.00 (s, 3 H); \text{^13C NMR:}\delta 209.9, 172.5, 57.1, 55.8, 54.2, 51.4, 43.4, 39.5, 28.7, 24.4,
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

16.7; HRMS (FAB) calculated for C_{13}H_{19}O_{3} [MH^{+}]: 223.1334, found: 223.1335. Recrystallization from petroleum ether 40–60/EtOAc afforded crystals suitable for X-ray analysis (see Table 2.2 for the crystal data).

3-(2-(2-Methyl-6-oxocyclohex-1-en-1-yl)ethyl)furan-2(5H)-one (38) To a solution of 37^5 (413 mg, 2.0 mmol) in a mixture of EtOH/CHCl_{3} (1:3, 15 mL) was added solid NaHCO_{3} (17 mg, 0.2 mmol, 10%) in one portion. After 5 min, N-bromosuccinimide (396 mg, 2.2 mmol, 1.1 equiv) was added in small portions and the mixture was stirred for 1.5 h. The reaction was quenched by the addition of brine (10 mL) and water (20 mL). The mixture was extracted with CHCl_{3} (3 × 10 mL) and the combined organic layers were washed with water (20 mL), dried over MgSO_{4} and concentrated in vacuo. The residue was dissolved in a mixture of acetone/water/HCl (99:1:0.1, 20 mL) and stirred overnight at room temperature. The reaction was quenched by the addition of solid NaHCO_{3} and filtered. The filtrate was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc 1:1) to give 38 (255 mg, 57%) as a yellow oil. R_f = 0.3 (petroleum ether 40–60/EtOAc 1:1); IR (neat): ν 2933, 1750, 1659 cm^{–1}; ^{1}H NMR: δ 7.19–7.18 (m, 1 H), 4.79–4.77 (m, 2 H), 2.57 (t, J = 7.6 Hz, 2 H), 2.59–2.31 (m, 6 H), 1.99–1.92 (m, 5 H); ^{13}C NMR: δ 198.5, 174.3, 156.9, 144.5, 133.9, 133.6, 70.0, 37.6, 32.7, 24.5, 23.1, 22.0, 21.1; HRMS (FAB) calculated for C_{13}H_{17}O_{3} [MH^{+}]: 221.1178, found: 221.1177.

Irradiation of photosubstrate 38 A solution of 38 (60 mg, 0.27 mmol) in a mixture of MeCN/acetone (9:1, 30 mL) was irradiated for 1.5 h at 300 nm. The mixture was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc 3:2). The chromatographic fractions containing cycloadduct 39 were combined and concentrated in vacuo. The residue was recrystallized from a mixture of cyclohexane/diethyl ether by slow evaporation of the solvent to give 39 (30 mg, 50%) as colorless needles, mp 100 °C; R_f = 0.28 (petroleum ether 40–60/EtOAc 3:2); IR (neat): ν 2925, 1759, 1688 cm^{–1}; ^{1}H NMR: δ 4.51 (dd, J = 10.4, 1.6 Hz, 1 H), 4.37 (dd, J = 10.4, 8.4 Hz, 1 H), 3.03 (dd, J = 8.0, 2.0 Hz, 1 H), 2.87 (dt, J = 11.2, 3.2 Hz, 1 H), 2.68–2.60 (m, 1 H), 2.42–2.24 (m, 3 H), 2.08–1.90 (m, 3 H), 1.78–1.65 (m, 2 H), 1.28 (s, 3 H); ^{13}C NMR: δ 205.7, 174.7, 66.5, 58.4, 47.3, 46.4, 42.1, 39.1, 30.7, 23.8, 23.2, 19.2, 18.8; HRMS (FAB) calculated for C_{13}H_{17}O_{3}...
[MH\(^+\)]: 221.1178, found: 221.1177; elemental analysis calculated for C\(_{13}\)H\(_{16}\)O\(_3\) (220.11): C, 70.89; H, 7.32. Found: C, 70.85; H, 7.38 (See table 2.2 for the crystal structure data).

4-(2-Methyl-6-oxocyclohex-1-enyl)-2-methylenebutyl acrylate (40)

To a solution of alcohol 26 (2.1 g, 11.0 mmol) in CH\(_2\)Cl\(_2\) (250 mL) was added Et\(_3\)N (3.1 mL, 22.0 mmol, 2.0 equiv) at 0 °C. Then a solution of acryloyl chloride (1.7 mL, 2.1 mmol, 1.9 equiv) in CH\(_2\)Cl\(_2\) (85 mL) was added dropwise. The ice bath was removed and the reaction mixture was stirred at room temperature for 2 h. The mixture was poured into ice water (250 mL). After separation the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (4 × 100 mL). The combined organic layers were dried over MgSO\(_4\) and concentrated \textit{in vacuo}. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 2:1) to give 40 (1.8 g, 65%) as a yellow oil. \(R_f = 0.42\) (petroleum ether 40–60/EtOAc 2:1); IR (neat): \(\nu\) 2934, 1722, 1655, 1626, 1404, 1379, 1294, 1267, 1179, 1049, 984, 910, 808 cm\(^{-1}\); \(^1\)H NMR: \(\delta\) 6.38 (dd, \(J = 17.3, 1.4\) Hz, 1 H), 6.10 (dd, \(J = 17.3, 10.4\) Hz, 1 H), 5.79 (dd, \(J = 10.4, 1.4\) Hz, 1 H), 4.98 (s, 1 H), 4.91 (s, 1 H), 4.59 (s, 2 H), 2.39 (t, \(J = 7.7\) Hz, 2 H), 2.32–2.27 (m, 4 H), 2.00 (t, \(J = 8.8\) Hz, 2 H), 1.90–1.83 (m, 5 H); \(^{13}\)C NMR: \(\delta\) 198.2, 165.6, 155.6, 143.5, 134.6, 130.7, 128.1, 112.3, 66.6, 37.6, 32.6, 32.1, 23.5, 22.0, 20.9; HRMS (FAB) calculated for C\(_{15}\)H\(_{21}\)O\(_3\) [MH\(^+\)]: 249.1491, found: 249.1491.

4-(2-(2-Methyl-6-oxocyclohex-1-enyl)ethyl)furan-2(5H)-one (41)

To a solution of 40 (1.8 g, 7.1 mmol) in CH\(_2\)Cl\(_2\) (710 mL) was added a 0.01 M solution of Grubbs’ first generation catalyst (587 mg, 0.71 mmol, 10%) in CH\(_2\)Cl\(_2\) (70 mL) over a period of 4 h using a syringe pump. Then the reaction mixture was warmed to reflux and stirred overnight. The mixture was allowed to cool to room temperature and concentrated \textit{in vacuo}. The residue was purified by chromatography (CH\(_2\)Cl\(_2\)/acetone 15:1) to give 41 (975 mg, 69%) as a crystalline solid, mp 67–68 °C; \(R_f = 0.28\) (CH\(_2\)Cl\(_2\)/acetone 15:1); IR (neat): \(\nu\) 2914, 1736, 1657, 1633 cm\(^{-1}\); \(^1\)H NMR: \(\delta\) 5.85 (t, \(J = 1.5\) Hz, 1 H), 4.78 (d, \(J = 1.5\) Hz, 2 H), 2.58 (t, \(J = 7.4\) Hz, 2 H), 2.46–2.37 (m, 6 H), 1.98–1.94 (m, 5 H); \(^{13}\)C NMR: \(\delta\) 198.3, 173.9, 169.9, 156.8, 133.4, 115.4, 72.9, 37.5, 32.7, 27.6, 23.1, 21.9, 21.1; HRMS (FAB) calculated for C\(_{13}\)H\(_{17}\)O\(_3\) \([\text{MH}^+]\): 221.1178, found: 221.1177; elemental analysis calculated for C\(_{13}\)H\(_{18}\)O\(_3\) (220.11): C, 70.89; H, 7.32. Found: C, 70.82; H, 7.35.
Irradiation of Photosubstrate 41 A solution of 41 (40 mg, 0.2 mmol) in a mixture of MeCN/acetone (9:1, 30 mL) was irradiated for 18 h at 300 nm. The mixture was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc 1:1) to give 42 (2 mg, 5%) as a crystalline solid, mp 102–103 °C; R_f = 0.4 (petroleum ether 40–60/EtOAc 1:1); IR (neat): v 2955, 1763, 1680 cm⁻¹; ¹H NMR: δ 4.33 (d, J = 11.3 Hz, 1 H), 3.94 (d, J = 11.3 Hz, 1 H), 2.95 (s, 1H), 2.77–2.68 (m, 1 H), 2.34–2.24 (m, 5 H), 2.05–1.98 (m, 1 H), 1.80–1.68 (m, 3 H), 1.50 (s, 3 H); ¹³C NMR: δ 210.3, 176.3, 71.6, 56.5, 52.2, 47.9, 42.1, 40.0, 33.3, 25.3, 24.9, 19.5, 18.6; HRMS (FAB) calculated for C₁₃H₁₇O₃ [MH⁺]: 221.1178, found: 221.1175

6-Iodo-7-methyl-1,4-dioxaspiro[4.5]dec-6-ene (44) To a solution of iodide 43 (120 mg, 0.51 mmol) and ethylene glycol (0.45 ml, 8 mmol, 16 equiv) in benzene (11 mL) was added a catalytic amount of p-TsOH•H₂O. The reaction mixture was warmed to reflux under Dean Stark conditions for 18 h. Then the reaction mixture was allowed to cool to room temperature and quenched by the addition of saturated aqueous NaHCO₃ (15 mL). The aqueous layer was extracted with diethyl ether (10 mL) and the combined organic layers were washed with brine (10 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (diethyl ether/petroleum ether 40–60 1:9 to 2:8) to give 44 (136 mg, 94%) as white crystals, mp 76–77 ºC; IR (neat): ν 2948, 2932, 2879, 1677, 1434 cm⁻¹; ¹H NMR: δ 4.23–4.21 (m, 2 H), 3.99–3.96 (m, 2 H), 2.19 (t, J = 3.6 Hz, 2 H), 1.95 (s, 3 H), 1.90–1.87 (m, 2 H), 1.78–1.72 (m, 2 H); ¹³C NMR: δ 146.9, 107.0, 106.0, 65.3, 33.8, 33.1, 29.8, 29.5, 20.2; HRMS (FAB) calculated for C₉H₁₄O₂I [MH⁺]: 281.0039, found: 281.0037

4-(7-Methyl-1,4-dioxaspiro[4.5]dec-6-en-6-yl)butanenitrile (45) To a solution of Pd(dba)₂ (107 mg, 0.18 mmol, 10 mol%) in THF (2 mL) was added SPhos (148 mg, 0.36 mmol, 20 mol%) and stirred for 5 min at room temperature under argon. Then a solution of 3-cyanopropylzinc bromide (5.2 mL, 0.5 M in THF, 2.6 mmol, 1.4 equiv) was added followed by the addition of iodide 44 (500 mg, 1.8 mmol). The mixture was warmed to reflux and stirred for 1 h. The reaction mixture was allowed to cool to room temperature and Et₃N was added. Then the mixture was concentrated in vacuo and the residue purified by chromatography (petroleum ether 40–60/EtOAc 5:1) to give 45 (290

53
mg, 73%) as a light yellow oil. IR (neat): ν 2930, 2878, 2244 cm⁻¹; ¹H NMR: δ 3.82–3.78 (m, 2 H), 3.66–3.63 (m, 2 H), 2.21 (t, J = 9.5 Hz, 2 H), 1.83–1.80 (m, 1 H), 1.76–1.69 (m, 6 H), 1.63–1.59 (m, 2 H); ¹³C NMR (C₆D₆): δ 136.4, 130.2, 119.6, 108.1, 64.3, 33.2, 31.6, 25.5, 25.3, 20.2, 19.1, 16.4; HRMS (FAB) calculated for C₁₃H₂₀NO₂ [MH⁺]: 222.1494, found: 222.1494.

3-Hydroxy-2-(2-(2-methyl-6-oxocyclohex-1-en-1-yl)ethyl)pentanenitrile (46) A solution of diisopropyl amine (91 µL, 0.65 mmol, 1.4 equiv) in THF (3 mL) was cooled to –78 °C. Then n-BuLi (338 µL, 1.6 M in hexanes, 0.54 mmol, 1.2 equiv) was added dropwise. The mixture was allowed to warm to –40 °C and cooled back to –78 °C. Then a solution of 45 (100 mg, 0.45 mmol) in THF (4.5 mL) was added dropwise. The mixture was allowed to warm to –40 °C and cooled back to –78 °C. Then a solution of propanal (49 µL, 0.67 mmol, 1.5 equiv) in THF (1 mL) was added dropwise. The mixture was left to stir for 2 h allowing it to warm to –30 °C. Then the reaction mixture was quenched by the addition of aqueous HCl and the mixture was allowed to warm to room temperature. The mixture was extracted with EtOAc (2 × 10 mL) and the combined organic layers were washed with saturated aqueous NaHCO₃, brine and dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 6:4) to give 46 (71 mg, 67%) as a light yellow oil. IR (neat): ν 3446, 2935, 2875, 2238, 1650, 1625 cm⁻¹; ¹H NMR: δ 3.79–3.76 (m, 0.4 H), 3.69–3.65 (m, 0.6 H), 2.67–2.61 (m, 1 H), 2.50–2.30 (m, 8 H), 2.01 (s, 3 H), 1.98–1.92 (m, 2 H), 1.82–1.50 (m, 5 H), 1.07–0.99 (m, 3 H); ¹³C NMR: δ 199.4, 198.9, 157.5, 157.2, 133.8, 133.6, 120.6, 120.0, 72.1, 71.7, 38.3, 37.9, 37.5, 37.4, 32.7, 28.3, 28.2, 27.4, 26.6, 22.8, 22.0, 21.9, 21.2, 21.1; HRMS (FAB) calculated for C₁₄H₂₂NO₂ [MH⁺]: 236.1651 found: 236.1651.

2-(2-(2-Methyl-6-oxocyclohex-1-en-1-yl)ethyl)pent-2-enenitrile (47) A solution of alcohol 46 (67 mg, 0.24 mmol) in CH₂Cl₂ (2 mL) was cooled to 0 °C. Then methanesulfonyl chloride (28 µL, 0.29 mmol, 1.2 equiv) was added followed by the dropwise addition of Et₃N (39 µL, 0.29 mmol, 2.1 equiv). The mixture was stirred at 0 °C and quenched by the addition of water (2 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2 × 5 mL). The combined organic layers were dried over MgSO₄ and concentrated in vacuo to afford the crude mesylate which
was used without further purification. The mesylate was dissolved in THF (2 mL) and cooled to 0 °C. Then DBU (108 µL, 0.72 mmol, 3 equiv) was added dropwise. The mixture was allowed to warm to room temperature and left to stir overnight. Then the solvent was removed *in vacuo* and the residue purified by chromatography (petroleum ether 40–60/EtOAc 9:1) to give 47 (34 mg, 54%) as a light yellow oil. IR (neat): ν 2934, 2873, 2214, 1660, 1628 cm\(^{-1}\); \(^1\)H NMR: δ 6.33 (t, \(J = 12.0\) Hz, 0.4 H), 6.13 (t, \(J = 12.0\) Hz, 0.6 H), 2.51 (t, \(J = 8.0\) Hz, 2 H), 2.42–2.20 (m, 8 H), 2.00–1.92 (m, 5 H), 1.07–1.01 (m, 3 H); 13C NMR: δ 198.6, 157.0, 150.3, 149.7, 133.5, 120.4, 117.9, 113.8, 113.5, 37.7, 33.3, 32.9, 27.8, 24.9, 24.4, 22.2, 22.1, 21.9, 21.4, 13.2, 13.1; HRMS (FAB) calculated for C\(_{14}\)H\(_{20}\)NO \([\text{MH}^+]: 218.1545\) found: 218.1545.

**Irradiation of photosubstrate 47** A solution of 47 (16 mg, 0.07 mmol) in a mixture of MeCN/acetone (9:1, 10 mL) was irradiated according to the general procedure for 2 h. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 95:5) to give two chromatographic fractions.

The first fraction provided 49 (5 mg, 31%) as a colorless oil. IR (neat): ν 2218, 1690, 1460 cm\(^{-1}\); \(^1\)H NMR: δ 2.94–2.89 (m, 1 H), 2.59–2.44 (m, 4 H), 2.32–2.24 (m, 1 H), 2.14–2.01 (m, 3 H), 1.77–1.69 (m, 4 H), 1.17 (s, 3 H), 0.98 (t, \(J = 7.2\) Hz, 3 H); 13C NMR: δ 206.0, 119.0, 57.9, 53.3, 44.3, 39.8, 38.4, 30.0, 29.1, 22.0, 20.1, 19.5, 18.2, 12.0. HRMS (FAB) calculated for C\(_{14}\)H\(_{20}\)ON \([\text{MH}^+]: 218.1545\), found: 218.1546

The second fraction provided 48 (9 mg, 56%) as a colorless oil. IR (neat): ν 2227, 1694 cm\(^{-1}\); \(^1\)H NMR: 5.32 (t, \(J = 7.3\) Hz, 1 H), 2.64–2.29 (m, 4 H), 2.21–2.02 (m, 2 H), 2.01–1.84 (m, 5 H), 1.77–1.59 (m, 2 H), 1.41–1.23 (m, 3 H), 1.02 (s, 3 H), 0.86 (t, \(J = 7.4\) Hz, 3 H); 13C NMR: δ 208.1, 118.8, 60.2, 54.8, 54.0, 41.4, 39.0, 27.6, 26.6, 24.1, 20.4, 18.2, 16.2, 10.8; HRMS (FAB) calculated for C\(_{14}\)H\(_{20}\)ON \([\text{MH}^+]: 218.1545\), found: 218.1546
(E)-Methyl-4-hydroxy-4-(7-methyl-1,4-dioxaspiro[4.5]dec-6-en–6–yl)but–2–enoate (53) A solution of iodide 44 (2.8 g, 10 mmol) in THF (56 mL) was cooled to –78 °C followed by the dropwise addition of n-BuLi (6.56 mL, 1.6 M in hexanes, 10.5 mmol, 1.05 equiv). The reaction mixture was stirred for 30 min. A solution of aldehyde 52 (1.37 g, 12 mmol, 1.2 equiv) in THF (28 mL) was added dropwise. After 3 hours the reaction was quenched by addition of 20% aqueous NaH2PO4 (10 mL). The organic layer was washed with saturated aqueous NaHCO3 (2 × 25 mL), water (25 mL), brine (25 mL), dried over MgSO4 and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 3:1) to give 53 (1.4 g, 64%) as a bright yellow oil. IR (neat): ν 1271; 1435; 1656; 1722; 2951; 3439 cm–1; 1H NMR: δ 7.05 (dd, J = 15.7, 3.3 Hz, 1 H), 5.98 (dd, J = 15.7, 2.3 Hz, 1 H), 5.04 (br s, 1 H), 3.92–3.82 (m, 4 H), 3.65 (s, 3 H), 3.31 (br s, 1 H), 2.01–1.97 (m, 2 H), 1.74 (s, 3 H), 1.72–1.69 (m, 1 H), 1.64–1.60 (m, 3 H); 13C NMR: δ 167.3, 151.5, 142.4, 129.7, 116.9, 109.0, 68.6, 64.0, 63.5, 51.2, 32.6, 32.5, 19.8, 19.5; HRMS (FAB) calculated for C14H21O5 [MH+]: 269.1389, found: 269.1387

(E)-Methyl 4-(tert-butyldimethylsilyloxy)-4-(7-methyl-1,4-dioxaspiro[4.5]dec-6-en-6-yl)but-2-enoate (54) A solution of 53 (1.2 g, 4.5 mmol) in DMF (10 mL) was cooled to 0 ºC. To this solution were added imidazole (1.2 g, 17.9 mmol, 4 equiv) and TBSCl (1.35 g, 8.9 mmol, 2 equiv). The reaction mixture was warmed to 50 ºC and stirred for 20 h. Then the reaction mixture was cooled to 0 ºC and quenched by the addition of MeOH (0.36 mL). The reaction mixture was diluted with diethyl ether (200 mL) and washed with saturated aqueous NaHCO3 (40 mL), water (2 × 40 mL), brine (25 mL), dried over MgSO4 and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 3:1) to give 54 (1.2 g, 72%) as white crystals, mp 98–99 ºC; Rf = 0.48 (petroleum ether 40–60/EtOAc 9:1); IR (neat): ν 2954 2858 1726 1662 1261 836 cm–1; 1H NMR: δ 7.04 (dd, J = 15.5, 3.1 Hz, 1 H), 6.08 (dd, J = 15.5, 2.3 Hz, 1 H), 4.9 (t, J = 2.6 Hz, 1 H), 4.01–3.96 (m, 4 H), 3.72 (s, 3 H), 1.94–1.93 (m, 2 H), 1.71 (s, 3 H), 1.65–1.59 (m, 4 H), 0.90 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H); 13C NMR: δ 167.8, 152.1, 142.8, 129.8, 117.0, 108.3, 68.4, 64.4, 51.4, 33.0, 32.9, 25.9, 20.1, 20.1, 18.2, –5.0, –5.7; HRMS (FAB) calculated for C20H35O5Si [MH+]: 383.2254, found: 383.2253
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

Methyl 4-((tert-butyldimethylsilyl)oxy)-4-(7-methyl-1,4-dioxa spiro[4.5]dec-6-en-6-yl)butanoate (55) A stirred solution of 54 (700 mg, 1.85 mmol) in EtOAc containing n-butylamine (28 mL, 1.25 mL/L, 1.0 equiv) was purged, first with argon and followed by hydrogen. The reaction mixture was stirred and kept under a hydrogen atmosphere for 90 min. The reaction mixture was filtered over Celite and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 9:1) to give 55 (0.68 g, 98%) as white needles, mp 31–32 °C; R_f = 0.52 (petroleum ether 40–60/EtOAc 9:1); IR (neat): ν 1257; 1662; 1741; 2856; 2929 cm⁻¹; ¹H NMR: δ 4.19 (dd, J = 10.1, 3.7 Hz, 1 H), 3.99–3.93 (m, 4 H), 3.65 (s, 3 H), 2.50–2.46 (m, 1 H), 2.39–2.31 (m, 1 H), 2.04–1.99 (m, 1 H), 1.96–1.92 (m, 3 H), 1.87 (s, 3 H), 1.70–1.60 (m, 1 H), 0.87 (s, 9 H), 0.01 (s, 3 H), –0.03 (s, 3 H); ¹³C NMR: δ 174.4, 139.9, 133.2, 108.6, 68.6, 64.5, 51.3, 33.4, 33.1, 33.0, 31.5, 25.9, 20.8, 20.3, 18.1, –4.9, –5.9. HRMS (FAB) calculated for C_{20}H_{37}O_{5}Si [MH⁺]: 385.2410, found: 385.2412

Methyl 4-((t-butyldimethylsilyloxy)-2-formyl-4-(7-methyl-1,4-dioxa spiro[4.5]dec-6-en-6-yl)-butanoate (56) To a solution of LDA (0.82 mmol, 1.05 equiv) in THF (5 mL) at –78 °C, was added dropwise a solution of 55 (300 mg, 0.78 mmol) in THF (5 mL). The reaction mixture was stirred for 30 min and freshly distilled methyl formate (40 µL, 1.56 mmol, 2 equiv) was added. The reaction mixture was stirred for 30 min and quenched by the addition of 20% aqueous NaH₂PO₄ (0.4 mL) and allowed to warm to room temperature. The reaction mixture was diluted with EtOAc (10 mL), washed with saturated aqueous NaHCO₃ (5 mL), water (5 mL), brine (5 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 9:1) to give 56 (280 mg, 88%) as a complex mixture of isomers as a colorless oil. R_f = 0.4 (petroleum ether 40–60/EtOAc 9:1); IR (neat): ν 3313, 2952, 2930, 2888, 2856, 2360, 1741, 1664, 1446, 1278, 1253, 1080 cm⁻¹; ¹H NMR: δ 11.43 (d, J = 12.5 Hz, 1 H), 9.71 (dd, J = 14.9, 2.8 Hz, 1 H), 6.99 (d, J = 12.5 Hz, 1 H), 4.21–4.13 (m, 3 H), 3.91–4.00 (m, 12 H), 3.66–3.89 (m, 9 H), 2.84–2.73 (m, 3 H), 2.43–2.51 (m, 3 H), 2.21–2.15 (m, 12 H), 1.85–1.94 (m, 12 H), 1.60–1.71 (m, 12 H), 0.91–0.83 (m, 27 H), 0.03–0.08 (m, 18 H); ¹³C NMR: δ 197.8, 197.6, 172.9, 170.1, 162.8, 162.3, 140.8, 139.8, 137.0, 133.1, 132.5, 108.8, 101.7, 68.3,
Methyl 4-((tert-butyldimethylsilyl)oxy)-4-(7-methyl-1,4-dioxa
spiro[4.5]dec-6-ene-6-yl)-2-methylenebutanoate (57) A solution of
potassium tert-butoxide (0.88 mmol, 1.2 equiv) in THF (10 mL) was
cooled to –20 °C and a solution of 56 (300 mg, 0.73 mmol) in THF (6 mL) was added. After 5
min Comins’ reagent (0.73 g, 0.95 mmol, 1.3 equiv) was added and the reaction mixture was
stirred for 2 hours. Then the reaction was quenched by the addition of saturated aqueous
NaHCO₃ (1 mL) and EtOAc was added. The organic layer was washed with saturated aqueous
NaHCO₃ (2 × 20 mL), water (10 mL), brine (10 mL), dried over MgSO₄ and concentrated in vacuo. The crude triflate was taken up in DMF (12 mL) and LiCl (93 mg, 2.2 mmol, 3 equiv),
triethylsilane (0.35 mL, 2.2 mmol, 3 equiv) and Pd(PPh₃)₄ (0.17 g, 0.15 mmol, 20 mol%) were
added. The mixture was warmed to 55 °C and stirred for 3 h. Then the reaction mixture was
cooled to 0 °C and diethyl ether (10 mL) was added. The organic phase was washed with
saturated aqueous NaHCO₃ (2 ×10 mL), water (10 mL), dried over MgSO₄ and concentrated in vacuo. The residue was purified by chromatography (petroleum ether 40–60/EtOAc 9:1) to give
57 (180 mg, 62%) as a colorless oil. \( R_f = 0.49 \) (petroleum ether 40–60/EtOAc 9:1); IR (neat): ν
2951, 2932, 2857, 1724, 1666, 1630, 1439, 1334, 1254, 1148, 1086 cm⁻¹; \(^1\)H NMR: \( \delta \)
6.16 (d, \( J = 1.8 \) Hz, 1 H), 5.55 (d, \( J = 1.7 \) Hz, 1 H), 4.41 (br s, 1 H), 4.00–3. 96 (m, 4 H), 3.72 (s, 3 H),
2.67 (d, \( J = 3.5 \) Hz, 2 H), 1.96–1.92 (m, 4 H), 1.71–1.65 (m, 2 H), 1.61 (br s, 3 H), 0.80 (s, 9 H),
–0.10 (s, 6 H); \(^{13}\)C NMR: \( \delta \) 167.7, 139.8, 138.5, 133.4, 127.0, 108.7, 68.6, 64.6, 63.7, 51.3, 40.9,
39.2, 33.6, 33.0, 25.8, 22.2, 20.8, 20.4, 18.0, –4.9; –5.9.

Methyl 4-((tert-butyldimethylsilyl)oxy)-4-(2-methyl-6-oxo

cyclohex-1-en-1-yl)-2-methylenebutanoate (58) To a stirred solution of
57 (180 mg, 0.45 mmol) in CH₂Cl₂ (2 mL) was added silica gel (600 mg)
and water (80 μL). The reaction mixture was stirred for 3 days and filtered. The filtrate was
concentrated in vacuo and the residue was purified by chromatography (petroleum ether 40–
60/EtOAc 9:1) to give 58 (100 mg, 63%) as a colorless oil. \( R_f = 0.28 \) (petroleum ether 40–
60/EtOAc 9:1); IR (neat): ν 2952, 2929, 2856, 1725, 1664, 1627, 1437, 1149, 1078 cm⁻¹; \(^1\)H
Intramolecular [2+2]-photocycloadditions of 2-(3-alkenyl)-3-methyl-2-cyclohexenones

NMR: δ 6.14 (d, J = 1.6 Hz, 1 H), 5.53 (s, 1 H), 5.21 (t, J = 6.8 Hz, 1 H), 3.75 (s, 3 H), 2.78–2.73 (m, 1 H), 2.45 (dd, J = 13.2 Hz, 6.0 Hz, 1 H), 2.33–2.30 (m, 4 H), 2.17 (br s, 3 H), 1.91–1.85 (m, 2 H), 0.81 (s, 9 H), −0.04 (s, 3 H); −0.13 (s, 3 H); 13C NMR: δ 197.6, 167.6, 137.7, 137.0, 127.1, 66.6, 51.7, 39.2, 37.8, 34.0, 25.8, 22.2, 21.7, 18.0, −5.0, −5.3.

Irradiation of photosubstrate 58 A solution of 58 (50 mg, 0.14 mmol) in a mixture of MeCN/acetonitrile (9:1, 30 mL) was irradiated for 2 h at 300 nm. The mixture was concentrated *in vacuo* and the residue purified by chromatography (petroleum ether 40–60/EtOAc 85:15) to give 59 (14 mg, 28%) as a colorless oil. *R* = 0.7 (petroleum ether 40–60/EtOAc 85:15); 1H NMR: δ 4.55 (dd, J = 7.7, 2.5 Hz, 1 H), 2.40 (s, 3 H), 2.66 (dd, J = 7.9, 4.3 Hz, 1 H); 2.41–2.27 (m, 3 H), 2.05–1.97 (m, 2 H), 1.97–1.87 (m, 1 H), 1.62–1.59 (m, 2 H), 1.37–1.25 (m, 4 H), 0.87 (s, 9 H), 0.11 (s, 6 H); 13C NMR: δ 207.2, 171.9, 70.7, 61.0, 54.9, 53.6, 51.5, 42.4, 40.3, 39.4, 30.0, 25.7, 22.8, 18.9, 17.9, −5.2; HRMS (FAB) calculated for C19H33O4Si [MH+]: 353.2148, found: 353.2151
Table 2.2. Crystal data and structure refinements for 25, 36 and 39

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<td>Crystal color</td>
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<td>Translucent colorless</td>
<td>Translucent colorless</td>
</tr>
<tr>
<td>Crystal shape</td>
<td>Regular lump</td>
<td>Rough fragment</td>
<td>Regular platelet</td>
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<td>Crystal size</td>
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<td>$0.23 \times 0.21 \times 0.09 \text{ mm}$</td>
<td>$0.26 \times 0.19 \times 0.09 \text{ mm}$</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C$<em>{19}$H$</em>{23}$NO$_{6}$</td>
<td>C$<em>{13}$H$</em>{18}$O$_{3}$</td>
<td>C$<em>{13}$H$</em>{16}$O$_{3}$</td>
</tr>
<tr>
<td>Formula weight</td>
<td>361.38</td>
<td>222.27</td>
<td>220.26</td>
</tr>
<tr>
<td>Temperature</td>
<td>208(2) K</td>
<td>208(2) K</td>
<td>208(2) K</td>
</tr>
<tr>
<td>Radiation/ wavelength</td>
<td>MoK$_{\alpha}$ (graphite mon.) / 0.71073 Å</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crystal system, space group</td>
<td>Monoclinic, P2$_1$/c</td>
<td>Orthorhombic, P2$_1$2$_1$2$_1$</td>
<td>Orthorhombic, Pbca</td>
</tr>
<tr>
<td>Unit cell dimen.</td>
<td>$a = 14.1883(8)$ Å, $b = 7.7060(5)$ Å, $c = 17.0604$ Å, $\alpha = 90^\circ$, $\beta = 109.974(5)^\circ$, $\gamma = 90^\circ$</td>
<td>$a = 7.0855$ Å, $b = 8.5315(4)$ Å, $c = 18.9214$ Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$</td>
<td>$a = 11.4151(6)$ Å, $b = 18.9214$ Å, $c = 20.916(2)$ Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$</td>
</tr>
<tr>
<td>Volume</td>
<td>$1753.10(18)$ Å$^3$</td>
<td>$1143.80(14)$ Å$^3$</td>
<td>$2234.2(3)$ Å$^3$</td>
</tr>
<tr>
<td>Z/ calc. density</td>
<td>4 / 1.369 Mg/m$^3$</td>
<td>4 / 1.291 Mg/m$^3$</td>
<td>8 / 1.310 Mg/m$^3$</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.102 mm$^{-1}$</td>
<td>0.090 mm$^{-1}$</td>
<td>0.092 mm$^{-1}$</td>
</tr>
<tr>
<td>Diffractometer/ scan</td>
<td>Nonius KappaCCD with area detector/ $\phi$ and $\omega$ scan</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F(000)</td>
<td>768</td>
<td>480</td>
<td>944</td>
</tr>
<tr>
<td>$\Theta$ range</td>
<td>2.48 to 25.00°</td>
<td>2.15 to 27.50°</td>
<td>2.92 to 24.99°</td>
</tr>
<tr>
<td>Index ranges</td>
<td>$-16&lt;=h&lt;=16$</td>
<td>$-9&lt;=h&lt;=8$</td>
<td>$-10&lt;=h&lt;=11$</td>
</tr>
<tr>
<td>Reflections collected/ Unique</td>
<td>2694 / 3061</td>
<td>13097 / 2579</td>
<td>19435 / 1959</td>
</tr>
<tr>
<td>$R_{int}$</td>
<td>0.0558</td>
<td>0.0349</td>
<td>0.0325</td>
</tr>
<tr>
<td>Reflections observed</td>
<td>2280 [$F&gt;2\sigma(F)$]</td>
<td>2004 [$F&gt;2\sigma(F)$]</td>
<td>1525 [$F&gt;2\sigma(F)$]</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>SADABS multiscan correction (Sheldrick 1996)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F$^2$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Computing</td>
<td>SHELXL-97 (Sheldrick, 1997)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data/ restraint/ parameters</td>
<td>3061 / 0 / 319</td>
<td>2579 / 0 / 147</td>
<td>1959 / 0 / 209</td>
</tr>
<tr>
<td>Goodness-of-fit on F$^2$</td>
<td>1.151</td>
<td>1.108</td>
<td>1.112</td>
</tr>
<tr>
<td>SHELXL-97 weight para.</td>
<td>0.038500, 2.203500, 0.044100, 0.343900, 0.034800, 1.407000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final $R$ indices [$F&gt;2\sigma(F)$]</td>
<td>$R_I = 0.0680$, $wR^2 = 0.1277$</td>
<td>$R_I = 0.0574$, $wR^2 = 0.1035$</td>
<td>$R_I = 0.0506$, $wR^2 = 0.0996$</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>$R_I = 0.0983$, $wR^2 = 0.1393$</td>
<td>$R_I = 0.0815$, $wR^2 = 0.1117$</td>
<td>$R_I = 0.0815$, $wR^2 = 0.1079$</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.327 and -0.377 eÅ$^{-3}$</td>
<td>0.241 and -0.241 eÅ$^{-3}$</td>
<td>0.203 and -0.167 eÅ$^{-3}$</td>
</tr>
</tbody>
</table>
2.10 References and notes