Visible Light-Mediated Photochemical Reactions of 2-(2′-Alkenyloxy)cycloalk-2-enones

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ABSTRACT: The title compounds were prepared, and their reactivity was studied upon sensitized irradiation at λ = 420 nm. Thioxanthen-9-one was employed as the sensitizer at a loading of 10 mol % in small-scale reactions and of 2.5 mol % on a larger scale. Cyclohex-2-enones substituted by a 2′-propenyloxy, 2′-butenyloxy, 2′-pentenyloxy, or 2′-methyl-2′-propenyloxy group in the 2-position gave the products of an intramolecular [2 + 2] photocycloaddition. The reaction proceeded with high regioselectivity (crossed product) and perfect diastereoselectivity (nine examples, 34−99% yield). If the olefin in the tether was trisubstituted (3′-methyl-2′-butenyloxy), no cycloaddition was observed. Rather, a cyclization with subsequent hydrogen abstraction occurred (three examples, 65−86% yield). The results are consistent with a reaction course via a triplet enone intermediate and the formation of a 1,4-diradical by an initial cyclization. The analogous cyclopent-2-enones were less prone to an intramolecular reaction. Instead, decomposition or intermolecular [2 + 2] photocycloaddition reactions prevailed. In the latter event, two main products were identified (three examples, 30−43% yield), resulting either from a head-to-head [2 + 2]-photodimerization or from a twofold [2 + 2] photocycloaddition of the enone to the olefin. The latter reaction sequence generated pentacyclic products with a central [1,5]dioxocane ring. The structure assignment of the two product types was corroborated by a single-crystal X-ray analysis.

INTRODUCTION

Like most intramolecular cycloadditions, the [2 + 2] photocycloaddition benefits from an improved regioselectivity if the two reaction partners are linked by a suitable tether. Cyclic α,β-unsaturated ketones represent the most frequently used chromophores in these reactions and the preferred position for attachment of a tether is the α- or the β-position. For an α-substituted enone I (Scheme 1), the number m of atoms in the tether governs the regioselectivity. A preference toward a parallel approach of the two olefins is observed if three or four atoms link the two olefinic groups (m = 3, 4), and the photocycloaddition products II are frequently referred to as straight products. If the tether is short (m = 2) photocycloaddition products III prevail in which the two olefins approach each other in a crossed fashion. The regioselectivity can be understood by the mechanistic course of the reaction which involves an initial attack of the olefin on the photoexcited enone to a 1,4-diradical intermediate (vide infra). The first step of the cycloaddition is consequently a cyclization in which the formation of five-membered rings is preferred.

2-(2′-Alkenyloxy)cycloalk-2-enones with the general structure IV represent a relatively unexplored compound class in [2 + 2] photocycloaddition chemistry. Ikeda et al. performed experiments with three 2-allyloxy cyclohex-2-enones as substrates, employing a high-pressure mercury lamp as the light source.
source and acetone as the solvent. Crossed products (general structure V) were obtained in 53–63% yield and subsequent transformations of these products were intensively studied. We have now looked at an expanded set of substrates with two main objectives: (a) Instead of UV light it was attempted to perform the photochemical reactions with visible light. To this end, a suitable sensitizer was required which absorbs in the visible range and does not lead to any side reactions. While visible light-mediated, sensitized reactions of styrenes and related compounds have recently received broad attention, studies with cyclic enones have remained scarce. (b) It was expected that other reaction pathways might be feasible depending on the structure of the chromophore and the substitution pattern of the olefin. Most importantly, [2 + 2] photodimerization and hydrogen abstraction were foreseen as competing reactions which would in turn lead to intriguing new structures. The results of our experimental work are summarized in this account.

**RESULTS AND DISCUSSION**

Figure 1 provides an overview about the compounds we employed in the present study. With regard to the olefin component, three 2'-alkenylxy groups were employed, that is, a 2'-propenylxy (allyloxy) group (substrates 1), a 2'-methyl-2'-propenylxy (methallyloxy) group (substrates 2), and a 3'-methyl-2'-butenylxy (prenyloxy) group (substrates 3). With regard to the enone component, some substituted cyclic enones (substrates b, c, d, f) were probed as starting materials apart from the unsubstituted cyclohex-2-enones (substrates a) and cyclopent-2-enones (substrates e). Cyclohex-2-enones with (Z)- and (E)-substituted 2'-alkenylxy groups were also prepared but will be discussed in a later section.

Because the synthesis of 2-(2'-alkenylxy)-4,4-dimethylcyclohex-2-enones was low yielding only substrates 1d and 2d were synthesized but not 3d. In general, three approaches toward the [2 + 2] photocycloaddition precursors were taken. Starting from cyclic 1,2-diketones the alkenylxy group was introduced either by condensation with the respective allyl alcohol under acidic conditions (method A: TsOH in cyclohexane, reflux) or by nucleophilic substitution of an allyl bromide via the enolate (method B: K$_2$CO$_3$ in DMF, room temperature). Along these lines, 1,2-diketones 4a, 4b, 4e, and 4f (Figure 2) served as precursors for the respective 2-(2'-alkenylxy)cycloalk-2-enones 1a–3a, 1b–3b, 1e–3e, and 1f–3f. For the synthesis of substituted cyclohexenones 1c–3c and 1d, 2d epoxides 4c and 4d served as starting materials, which underwent nucleophilic substitution in position C2 when treated with an excess of allylic alcohol under basic conditions (method C: NaH or KOH as base). As mentioned above the reaction gave low yields (6–12%) when applied to epoxide 4d which limited the supply of the starting material. Reasons for the inefficiency of the procedure were difficulties in removing excess allylic alcohol and formation of a side product (see the Supporting Information for further details) by dimerization of the epoxide. Because the emphasis of the study was on the [2 + 2] photocycloaddition chemistry, alternative routes to the substituted enones were not pursued. With the exception of compounds 1a, 2a, and 1c, 2-(2'-alkenylxy)cycloalk-2-enones have not been previously employed in photochemical reactions.

Preliminary photochemical studies were performed with substrate 1a. Its triplet energy was determined from phosphorescence experiments (77 K, CH$_2$Cl$_2$) as $E_T = 235$ kJ mol$^{-1}$. Because a wavelength of $\lambda = 400$ nm corresponds to an energy of $0.300$ kJ Es$^{-1}$ (1 Es = 6.022 × 10$^{22}$ photons), it seemed feasible to promote the [2 + 2] photocycloaddition with visible light upon a judicious choice of a sensitizer. In this regard, parent thioxanthen-9-one ($S$) and its derivatives represent an excellent option and have been nicely exploited by Booker-Milburn and co-workers in [2 + 2] photocycloaddition reactions on a large scale. In recent works on visible light-mediated reactions, we have also seen that catalyst loadings can be as low as 1 mol % for a thioxanthenone sensitizer. Experiments with a selection of potential sensitizers (see the Supporting Information for details) confirmed the suitability of thioxanthen-9-one ($S$) as the catalyst in the planned reaction ($E_T = 268$ kJ mol$^{-1}$). Dichloromethane was established as the preferred solvent and there was no improvement in selectivity if the reaction was performed at low temperatures. The reactions were run on a small scale (50–200 μmol substrate, c = 10 mM) at a wavelength of $\lambda = 420$ nm (16 fluorescent lamps with an emission maximum at $\lambda = 420$ nm, for the emission spectrum, see the Supporting Information) and yields of product 8a (Scheme 2) were consistently around 70%, irrespective of whether 2.5, 5, or 10 mol % of $S$ were used. Indeed, the low-molecular weight (212 Da) of thioxanthen-9-one ($S$) made it relatively difficult to measure the exact quantity. Iridium catalysts (2.5 mol %) with a much higher molecular weight performed similar to $S$ and there was a correlation between the reaction time and the triplet energy of the catalyst. Sensitizers with a triplet energy $E_T > 250$ kJ mol$^{-1}$ led to a complete conversion after 2.5 h. The reaction time increased with a decrease in triplet energy. The reaction with Ir(ppy)$_3$ ($E_T = 231$ kJ mol$^{-1}$), for example, required 5 h before no substrate was detected by TLC. The ruthenium complex Ru-
Scheme 2. Mechanistic Proposal for the Course of the Sensitized Intermolecular [2 + 2] Photocycloaddition of Cyclohex-2-enone 1a

(E1/2 red ≤ −2.0 V)18 render any single electron transfer (photoredox) processes not viable.

Several allyloxy- and methallyloxy-substituted cycloalk-2-enones reacted similar to substrate 1a, and the results are summarized in Scheme 3. In order to secure a reproducible reaction course, 10 mol % of the sensitizer were used for small scale reactions. Some of the reactions were also performed on a larger scale (1 mmol) and at a higher concentration (c = 25 mM). In this case, only 2.5 mol % of the sensitizer were employed. Despite a longer reaction time, chemoselectivity did not suffer and the yields were as good as on a small scale or even higher.

Crossed photocycloaddition products 8a–8c and 9a–9c were isolated cleanly without any indication for the formation of other side products. Among the 4,4-dimethylcyclohexenones 1d and 2d, only the latter substrate showed a photochemical reaction. The former substrate did not react and the starting material was recovered. Because quantities were limited, the low yield of product 9d might be associated with the loss of the product during chromatographic purification. Both compounds 9d and 9e were difficult to detect on TLC which further impaired a quantitative isolation. Cyclpentenone 1e was converted upon sensitized irradiation (cf. Scheme 3) but no defined products could be isolated. The same observation was made when the compound was irradiated directly at λ = 350 nm (c = 10 mM, CH2Cl2).

The suspected intermediacy of 1,4-diradicals in the course of the [2 + 2] photocycloaddition implied the possibility to perform stereoconvergent reactions with 1,2-disubstituted olefins in the tether. Substrates E-10/Z-10 (Scheme 4) were obtained from an E/Z-mixture (d.r. = 50/50) of crotyl alcohol (2-butanol) by condensation with 1,2-diketone 4a (method A). Sensitized irradiation delivered photocycloaddition product 11 as a single diastereoisomer accompanied by an olefinic impurity which was removed by treatment with 3,6-bis-(methoxycarbonyl)-1,2,4,5-tetrazine.21 The yield of the clean isolated product was 78% and its relative configuration was assigned based on NOESY spectra (see the Supporting Information for further details).

The ethyl-substituted substrates 12 were obtained in a diastereomERICally pure form from (E)- and (Z)-3-penten-1-ol and diketone 4a. The compounds were individually subjected to the irradiation conditions and delivered the same product 13. In this case, the product was not completely homogenous but was contaminated by compound 14 (yield from E-12: quant., 13/14 = 82/18; yield from Z-12: 90%, 13/14 = 83/17). Byproduct formation is likely to occur from the intermediate 1,4-diradical by intramolecular hydrogen abstraction (vide infra). It was possible to remove the undesired compound by oxidation and the desired product 13 was obtained in 69% yield. The outcome of the reactions suggests that 1,4-diradicals related to 6 are the major intermediates in the [2 + 2] photocycloaddition to products 11 and 13. Not only do they explain the observed stereoconvergence of the reaction but they also account for the formation of the olefinic side products.

Yield if the reaction was performed on a 1 mmol scale.

Obtained from an E/Z-mixture (d.r. = 50/50) of crotyl alcohol (2-butanol) by condensation with 1,2-diketone 4a (method A). Sensitized irradiation delivered photocycloaddition product 11 as a single diastereoisomer accompanied by an olefinic impurity which was removed by treatment with 3,6-bis-(methoxycarbonyl)-1,2,4,5-tetrazine.21 The yield of the clean isolated product was 78% and its relative configuration was assigned based on NOESY spectra (see the Supporting Information for further details).

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When cyclohexenones 3a−3c with a trisubstituted tethered olefin were employed as starting materials, a cyclization/reduction pathway became dominant and [2 + 2] photocycloaddition products were not detected. The high yields achieved for products 16a−16c (Scheme 5) render some synthetic utility to this method, which represents formally a conjugate addition to the β-carbon atom of the α,β-unsaturated enone. The assignment of the relative product configuration was suggested by 1H NMR coupling constants and NOESY experiments (see the Supporting Information for details) and the selectivity of the process is remarkable as it allows to construct three contiguous stereogenic centers with a defined configuration.

Mechanistically, the first step of the sequence occurs presumably in analogy to the C−C bond forming event previously mentioned (1a → 6), that is, the triplet of 3 undergoes intramolecular addition to the tethered olefin by a five-membered ring cyclization. However, because of steric hindrance of the substituents (R3 and CMe2), bond formation occurs in a trans fashion. In the intermediate bicyclic 1,4-diradical 15 cyclization to a cyclobutane by C−C bond formation is not feasible, but an intramolecular hydrogen abstraction3 can readily occur which generates products 16.

Like cyclopentenone 1e in the [2 + 2] photocycloaddition study, the cyclopentenone with a prenyloxy substituent (3e) showed only decomposition under the conditions successfully employed for substrate 3a. Also the cyclopentenones 1f−3f with an additional methyl group in the β-position displayed a reactivity that did not parallel the reactivity pattern of the comparable six-membered cyclic enones 1b−3b. In this instance, however, defined products could be isolated albeit in only low to moderate yields. The preferred reaction pathway of the cyclopentenones 1f−3f was a [2 + 2] photodimerization with the interesting twist that there are two double bonds available in each component. Along these lines, 2-(2′-propenylxlyoxy)-3-methylcycloalk-2-enone (1f) produced a set of [2 + 2] photocycloaddition products from which two products 17 and 18 could be isolated (Scheme 6). Product 17 is the [2 + 2] photodimerization product resulting from the addition of the two enone double bonds in what is commonly referred to as a cis-anti-cis addition.12 The cis fusion between the five-membered rings and the four-membered ring is to be expected because of the rigidity of the skeleton, while the anti (trans) configuration of the cyclopentanone rings minimizes their steric repulsion. Based on its NMR data, second product 18 was also symmetric and—as confirmed by its crystal structure—it displays an inversion center (S2 symmetry).22 The crystal structure revealed that the bicyclo[3.2.0]heptane core is cis connected and all substituents within the cyclobutane are positioned in a cis fashion. The two constitutionally identical bicyclo[3.2.0]heptane fragments possess an opposite absolute configuration. Given the low combined yield for compounds 17 and 18, it is likely that other dimerization products were formed but could not be isolated in a pure form. [2 + 2] Photodimerization, in a head-to-head fashion, is common for cyclopentenones,23 while the regioselectivity of the intermolecular head-to-head double bond addition of a monosubstituted olefin to an enone has less precedence.9d,23d,24

The overall product yield achieved in the [2 + 2] photodimerization of compound 2f was slightly higher (44%) than observed for 1f. Again two regioisomers were isolated, one of which was the enone dimerization product 19 and the other the product of an enone/olefin addition. The configuration assignment for the latter product 20 was based on an analogy to product 18 (Scheme 7).

Scheme 6. [2 + 2] Photodimerization of Cyclopent-2-enone 1f and Crystal Structure** of Product 18

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**Ellipsoids in the ORTEP structure are displayed at the 50% probability level.
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Scheme 7. [2 + 2] Photodimerization of Cyclopent-2-enone 2f to Products 19 and 20

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Remarkably, even prenyloxy-substituted enone 3f did not display the cyclization tendency observed with cyclohexenones 3a−3c. Instead, the only product isolated from its sensitized irradiation was the head-to-head regioisomer 21 of a [2 + 2] photodimerization that was obtained in 34% yield. The C2-symmetric compound displayed the same relative configuration as the previously discussed enone dimers 17 and 19, and the structure assignment could in this specific case be secured by a single-crystal structure analysis (Figure 3).

The difference between the cyclopentenone and the cyclohexenone chromophore in the photochemical reactivity of their 2-(2′-alkenloxy)-substituted derivatives is remarkable. Only in a single case (product 9e), an intramolecular attack of
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the tethered olefin occurred while with all other substrates there was no indication for such an attack, not even for a cyclization to a 1,4-diradical (in analogy to the formation of intermediate 15). The cyclization seems retarded and intermolecular [2 + 2] photocycloaddition reactions become competitive. The observation is important because it allows to access cyclopentenone dimers without protecting the olefinic side chains.

In summary, an array of structurally diverse products has been obtained by irradiation of the title compounds in the presence of a sensitizer. The photochemical reactions of all cyclohexenone derivatives proceeded in moderate to excellent yields and with a high degree of diastereoselectivity. Intramolecular reactions were observed exclusively either as [2 + 2] photocycloaddition or as a cyclization/hydrogen abstraction cascade. Up to four stereogenic centers can be established in a single reaction and the products hold promise as scaffolds which enable further functionalization at several positions. The cyclopentenone derivatives were less prone to intramolecular reactions but underwent preferentially an intermolecular reaction leading to [2 + 2] photodimerization products.

**EXPERIMENTAL SECTION**

**General Methods.** All air and moisture sensitive reactions were carried out in flame-dried glassware under an argon atmosphere using standard Schlenk techniques. For moisture sensitive reactions, tetrahydrofuran (THF), diethyl ether (EtO\(_2\)), and dichloromethane (CH\(_2\)Cl\(_2\)) were dried using a solvent purification system. Cyclohexane was dried over neutral aluminum oxide and stored over 4 Å molecular sieves. Dry N,N-dimethylformamide (DMF) was obtained in the highest available purity stored over molecular sieves and used without further purification. For photochemical reactions, dry dichloromethane was degassed by three freeze–pump–thaw cycles. Cooling baths were used with ice/water (0 °C) and dry ice/ethanol (−78 °C).

Technical solvents [1,2-dichloroethane (DCE), pentane (P), EtO\(_2\), CH\(_2\)Cl\(_2\), methanol (MeOH), ethyl acetate (EtOAc), cyclohexane] were distilled prior to use. Flash column chromatography was performed on silica 60 (230–400 mesh) and thin-layer chromatography (TLC) on silica-coated glass plates (silica 60 F\(_{254}\)) with detection by UV-light (\(\lambda = 254\) nm) and/or by staining (vanillin–H\(_2\)SO\(_4\) reaction leading to \([2 + 2]\) photodimerization products.

**General Procedure 1 (Method A).** To a solution of the respective 1,2-cyclohexadiene (1.0 equiv) in dry cyclohexane (40 mL/g starting material) was added \(p\)-TsOH·H\(_2\)O (3.0 mol %) and the corresponding allylic bromide (4.0 equiv). The reaction mixture was heated at reflux in a Dean–Stark apparatus for 15–17 h. The solution was allowed to cool to room temperature, washed with brine (2 × 50 mL/g), dried over Na\(_2\)SO\(_4\), and filtered. The solvent was removed under reduced pressure and the crude product was purified using flash column chromatography (P/EtO\(_2\)).

**General Procedure 2 (Method B).** To a solution of the respective 1,2-cyclohexadiene (1.0 equiv) in dry DMF (40 mL/g starting material) was added K\(_2\)CO\(_3\) (1.2 equiv) and the respective allylic bromide (1.2 equiv). The reaction mixture was stirred at room temperature for 4.5–21 h. The reaction was quenched by the addition of H\(_2\)O (20 mL/g). EtO\(_2\) (40 mL/g) was added and the layers were separated. The organic layer was washed with H\(_2\)O (4 × 40 mL/g) and brine (1 × 60 mL/g), dried over Na\(_2\)SO\(_4\), and filtered. The solvent was removed under reduced pressure and the crude product was purified using flash column chromatography (P/EtO\(_2\)).

**General Procedure 3 (Method C).** A round bottom flask charged with NaH (60 wt %, 1.2 equiv) was cooled to 0 °C and the respective allylic alcohol (30 equiv) was added dropwise. The reaction mixture was stirred for 10 min and subsequently the corresponding epoxide (1.0 equiv) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 20–24 h. The mixture was diluted with EtO\(_2\) (75 mL/g) and quenched by the addition of H\(_2\)O (35 mL/g). The layers were separated and the organic layer was washed with H\(_2\)O (1 × 35 mL/g) and brine (1 × 75 mL/g), dried over Na\(_2\)SO\(_4\), and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (P/EtO\(_2\)).

**General Procedure 4 (Method D).** To a solution of the respective 1,2-cyclopentadiene (1.0 equiv) in dry DMF (40 mL/g starting material) was added K\(_2\)CO\(_3\) (1.2 equiv) and the respective allylic bromide (1.2 equiv). The reaction mixture was stirred at room temperature for 17–22 h. The reaction was quenched by the addition of H\(_2\)O (20 mL/g). EtO\(_2\) (40 mL/g) was added and the layers were separated. The organic layer was washed with H\(_2\)O (4 × 40 mL/g) and brine (1 × 60 mL/g), dried over Na\(_2\)SO\(_4\), and filtered. The solvent was removed under reduced pressure and the crude product was purified using flash column chromatography (P/EtO\(_2\)).

**2-(Allyloxy)cyclohex-2-en-1-one (1a).** According to general procedure 1, compound 1a was synthesized starting from 4a (1.00 g, 8.92 mmol, 1.0 equiv), allylic alcohol (2.43 mL, 2.07 g, 35.7 mmol, 4.0 equiv), and \(p\)-TsOH·H\(_2\)O (51.3 mg, 270 \(\mu\)mol, 30 mol %). Purification by flash column chromatography (SiO\(_2\), P/EtO\(_2\) = 5/1, UV) afforded the product (667 mg, 4.38 mmol, 49% yield). TLC (P/EtO\(_2\) = 3/1): \(R_f = 0.18\) (UV, KMnO\(_4\)), \(1^1\)NMR (400 MHz, CDCl\(_3\), 300 K): \(\delta = 1.97\) (virt. quint., \(J = 6.2\) Hz, 2H), 2.41 (td, \(J = 6.0, 4.7\) Hz, 2H), 2.48–2.53 (m, 2H), 4.31 (virt. dt, \(J = 5.5\) Hz, \(J = 1.5\) Hz, 2H), 5.25 (ddt, \(J = 1.5\) Hz, \(J = 10.0\) Hz, \(J = 1.5\) Hz, 1H), 5.33 (ddt, \(J = 1.5\) Hz, \(J = 17.4\) Hz, \(J = 1.5\) Hz, 1H), 5.89 (t, \(J = 4.7\) Hz, 1H), 5.98 (ddt, \(J = 17.4\), 10.6, 5.5 Hz, 1H). \(1^1\)C\(_{18}\)NMR (101 MHz, CDCl\(_3\), 300 K): \(\delta = 23.1\) (t), 24.7 (t), 39.0 (t), 68.8 (t), 118.1 (t), 118.7 (d), 133.1 (d), 150.5 (s), 194.5 (s), UV/vis (CHCl\(_3\), \(c = 0.5\) mm): \(\lambda = 259\) nm (\(\varepsilon = 3736\) \(\mu\)mol L⁻¹ cm⁻¹). Data of this compound are in accordance with the literature.

**2-(Allyloxy)-3-methylcyclohex-2-en-1-one (1b).** According to general procedure 2, compound 1b was synthesized starting from 4a (500 mg, 3.96 mmol, 1.0 equiv), allyl bromide (410 \(\mu\)L, 580 mg, 4.76 mmol, 1.2 equiv), and K\(_2\)CO\(_3\) (670 mg, 4.85 mmol, 1.2 equiv). Purification by flash column chromatography (SiO\(_2\), P/EtO\(_2\) = 9/1, UV) afforded the product (259 mg, 1.56 mmol, 39%) as colorless oil.
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1. (Allyl)-2,3-methylcyclopropen-2-one (1f). According to general procedure 4, compound 1f was synthesized starting from 4f (500 mg, 4.46 mmol, 1.0 equiv), allyl bromide (460 μL, 650 mg, 5.35 mmol, 1.2 equiv), and K₂CO₃ (740 mg, 5.35 mmol, 1.2 equiv). Purification by flash column chromatography (SiO₂, P/Et₂O = 3/1, UV) afforded the product (387 mg, 2.54 mmol, 55%) as colorless oil. TLC (P/Et₂O = 3/1): Rf = 0.24 [UV, KMnO₄]. 1H NMR (500 MHz, CDCl₃, 300 K): δ 1.98 (s, 3H), 2.30–2.39 (m, 2H), 2.43 (virt. dt, 1J = 7.1 Hz, 1J̃ = 2.5 Hz, 1J̃̃ = 1.2 Hz, 2H), 4.67 (vrt. dt, 1J = 5.9 Hz, 1J̃ = 1.4 Hz, 2H). 1.2. (2-Methylallyloxy)cyclohex-2-en-1-one (2a). According to general procedure 2, compound 2a was synthesized starting from 4a (1.00 g, 8.92 mmol, 1.0 equiv), methyllithium (3.00 mL, 2.57 g, 35.7 mmol, 4.0 equiv), and p-TsOH·H₂O (52.3 mg, 275 μmol, 0.5 mol %). Purification by flash column chromatography (SiO₂, P/Et₂O = 9/1 → 4/1, UV) afforded the product (682 mg, 4.10 mmol, 46%) as colorless oil. TLC (P/Et₂O = 3/1): Rf = 0.19 [UV, KMnO₄]. 1H NMR (500 MHz, CDCl₃, 300 K): δ 1.36 (vrt. quint., 1J = 6.1 Hz, 2H), 1.66 (s, 3H), 1.74 (td, 1J = 6.0, 4.6 Hz, 2H), 2.05–2.21 (m, 2H), 3.90 (s, 2H), 4.86 (s, 1H), 5.11 (s, 1H), 5.30 (t, 1J = 4.6 Hz, 1H). 13C NMR (75 MHz, CDCl₃, 300 K): δ 18.9 (q), 23.5 (t), 24.8 (t), 39.6 (s), 71.9 (t), 113.0 (t), 118.1 (d), 141.6 (s), 151.5 (s), 190.4 (s). UV/vis (CHCl₃, c = 0.5 mm): λ = 259 nm (ε = 4518 cm⁻¹ M⁻¹). This data of the compound were in accordance with the literature. 2. (2-Methylallyloxy)cyclohex-2-en-1-one (2a). According to general procedure 2, compound 2a was synthesized starting from 4a (500 mg, 3.96 mmol, 1.0 equiv), methyllithium (480 μL, 640 mg, 4.76 mmol, 1.2 equiv), and K₂CO₃ (0.660 mg, 4.76 mmol, 1.2 equiv). Purification by flash column chromatography (SiO₂, P/Et₂O = 9/1 → 4/1, UV) afforded the product (412 mg, 2.09 mmol, 53%) as orange oil. TLC (P/Et₂O = 3/1): Rf = 0.24 [UV, KMnO₄]. 1H NMR (500 MHz, CDCl₃, 300 K): δ 1.82 (s, 3H), 1.90–1.98 (m, 5H), 2.38 (t, 1J = 6.1 Hz, 2H), 2.44 (t, 1J = 6.7 Hz, 2H), 4.22 (s, 2H), 4.90 (vrt. t, 1J̃̃ = 2.0 Hz, 1H), 5.02 (s, 1H). 13C NMR (126 MHz, CDCl₃, 300 K): δ 18.0 (q), 19.9 (q), 22.3 (t), 31.7 (t), 38.9 (s), 75.7 (t), 112.8 (t), 142.0 (s), 146.1 (s), 148.2 (s), 194.9 (s). IR (ATR) 𝜆 = 3290 (w), 1673 (m), 1594 (m), 1446 (s), 1479 (s), 1949 (s). MS (EI, 70 eV) 𝑚/𝑧 (%): 152 (49), 137 (76), 123 (19), 112 (9), 96 (22), 84 (18), 81 (8), 69 (26), 67 (15), 55 (19), 41 (100). HRMS (EI) 𝑚/𝑧: [M⁺] calced for C₅H₁₀O₂, 105.0827; found, 105.0823. UV/vis (CHCl₃, c = 0.5 mm): λ = 248 nm (ε = 10.13 cm⁻¹ M⁻¹).
alcohol (1.0 mL, 0.851 mg, 11.8 mmol, 13 equiv) was then added (w), 1368 (w), 1163 (m), 902 (w). MS (EI, 70 eV) m/z (%): 194 (57), 179 (18), 151 (9), 136 (22), 127 (14), 114 (13), 99 (100), 83 (93). HRMS (EI) m/z [M]+: [13C1H18O2, 195.1350]. 1H NMR (400 MHz, CDCl3, 300 K): δ 1.26 (3H, dd, J = 4.7 Hz, 2H), 2.36 (s, 2H). 4.18 (s, 2H), 4.94 (s, 1H). TLC (P/Et2O = 1/1): λ = 262 nm (ε = 4374 cm−2 M−1).

4.4-Dimethyl-2-[2-(methylallyl)oxy]cyclohex-2-en-1-one (2d). KOH (85 wt %, 59.9 mg, 0.980 mmol, 1.2 equiv) was dissolved in methylic alcohol (1.0 mL, 851 mg, 11.8 mmol, 13 equiv). A solution of epoxide 4d (127 mg, 908 mmol, 1.0 equiv) in methylic alcohol (1.0 mL, 0.851 mg, 11.8 mmol, 13 equiv) was then added dropwise, and the reaction mixture was stirred at room temperature overnight. Subsequently, the reaction mixture was diluted with 15 mL of EtO and quenched by the addition of 15 mL of H2O. The layers were separated and the aqueous layer was extracted with EtO (2 × 15 mL). The combined organic layers were washed with brine (1 × 50 mL), dried over Na2SO4, filtered, and the solvent as well as the remaining volatiles were removed under reduced pressure. After purification by flash column chromatography (SiO2, P/Et2O = 5/1), product 2d (11.0 mg, 56.6 μmol, 6%) was obtained as colorless oil. TLC (P/Et2O = 3/1): Rf = 0.37 [UV, K2MnO4]. 1H NMR (500 MHz, CDCl3, 300 K): δ 1.37 (d, J = 4.8 Hz, 2H), 2.36 (m, 2H), 4.18 (dd, J = 4.7 Hz, 2H), 2.36 (s, 2H), 4.18 (s, 2H), 4.94 (s, 1H). 1H NMR (101 MHz, CDCl3, 300 K): δ 18.2 (q), 22.4 (q), 25.8 (q), 28.2 (t), 29.8 (t), 31.7 (q), 31.7 (q), 32.7 (t), 36.4 (s), 73.0 (t). HRMS (EI) m/z [M]+ for C11H16O2: 182 (100), 141 (100), 87 (70), 61 (43), 35 (73). 1H NMR (500 MHz, CDCl3, 300 K): δ 1.37 (d, J = 4.6 Hz, 3H), 2.21 (s, 2H), 2.36 (s, 2H). 4.18 (s, 2H), 4.20 (d, J = 4.7 Hz, 2H), 2.36 (s, 2H). 4.18 (s, 2H), 4.94 (s, 1H). HRMS (EI) m/z [M]+ for C14H22O2: 224 (100), 183 (100), 142 (99), 80 (80), 79 (59), 77 (44), 76 (100), 45 (71), 33 (33), 32 (22), 31 (100), 30 (100), 29 (70), 13 (100), 11 (83).
mg, 2.73 mmol, 1.6 equiv) in 7.0 mL of dry DMF. The reaction was quenched by the addition of 7 mL of H2O and 15 mL of Et2O. The organic layer was washed with H2O (4 × 15 mL) and brine (1 × 30 mL), dried over Na2SO4, filtered, and the solvent was removed under reduced pressure. Purification by flash column chromatography (SiO2, P/Et2O = 3/1, UV) afforded the product (600.0 mg, 360.0 mmol, 21%) as a colorless solid. TLC (P/Et2O = 42–43, \[\nu\] 0.35 [UV, KmnO4]). 1H NMR (500 MHz, CDCl3, 300 K): \(\delta 1.07\) (s, 3H), \(\delta 1.76\) (s, 3H), 2.41–2.44 (m, 2H), 2.48–2.60 (m, 2H), 4.40 (d, \(\nu\) = 6.8 Hz, 2H), 5.43 (t, \(\nu\) = 6.8 Hz, 1H), 6.36 (virt. q, \(\nu\) \(\approx\) \(\delta\) = 2.5 Hz, 1H). 13C{1H} NMR (126 MHz, CDCl3, 300 K): \(\delta 18.3\) (q), \(22.2\) (t), \(25.9\) (q), \(33.2\) (t), \(66.7\) (t), \(119.1\) (d), \(127.6\) (d), \(138.7\) (s), \(156.6\) (s), \(199.8\) (s). Data of this compound were in accordance to the literature.21

According to a modified literature procedure:27 To an ice-cooled solution of 5,5-dimethylcyclohex-2-en-1-one (990 mg, 9.77 mmol, 1.0 equiv) in 16 mL of MeOH were dropwise added H2O2 (30 wt %, 3.30 mL, 11.0 g, 32.3 mmol, 4.1 equiv) and 6 M NaOH (0.64 mL, 154 mg, 3.84 mmol, 0.5 equiv). The reaction mixture was allowed to warm to room temperature and stirred for 2 h. Subsequently, the reaction mixture was diluted with 32 mL of CH2Cl2 and H2O was added until proper phase separation was achieved. The layers were separated and the aqueous layer was extracted with CH2Cl2 (3 × 30 mL). The combined organic layers were washed with brine (2 × 80 mL), dried over Na2SO4, filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO2, P/Et2O = 2/1), the product (901 mg, 643.8 mmol, 80%) was obtained as colorless oil. TLC (P/Et2O = 2/1): \(R_f\) = 0.56 [UV, KmnO4].

According to General Procedure 5 (Irradiation). Thiophane 5 (10 mol %) was dissolved in 1.0 mL of dry degassed CH2Cl2 and transferred to a flame dried Duran phototube. The respective 2-(2'-alkenyl) cycloalk-2-enone (1.0 equiv) dissolved in 1.0 mL of dry degassed CH2Cl2 was then added, and the reaction mixture was diluted with dry degassed CH2Cl2 until a concentration of 10 mM (relative to the substrate) was reached. The reaction mixture was irradiated at room temperature in a previously described irradiation setup21 (\(\lambda\) = 420 nm, for details about the light source, see the Supporting Information). Irradiation was continued until full conversion was reached and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (P/Et2O).

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https://dx.doi.org/10.1021/acs.joc.0c01501

*J. Org. Chem.* 2020, 85, 11426–11439
(3R,5aS,7aSR)-3a-Methylhexahydro-7H-3,7,3a-methano-benzofuran-7-one (8b). According to general procedure 5, compound 8b was synthesized starting from 1b (16.8 mg, 101 μmol, 1.0 equiv) and thioxanthone 5 (2.19 mg, 10.3 mol %) over 2 h. Purification by flash column chromatography (SiO2, P/Et2O = 1/2, KMnO4) afforded the product (15.2 mg, 91.2 μmol, 91%) as a colorless solid. Mp 38–47 °C. TLC (P/EtO = 1/2): Rf = 0.04 [KMnO4].

(3R,5aS,7aSR)-3-Methylhexahydro-7H-3,7,3a-methano-benzofuran-7-one (8a). According to general procedure 5, compound 8a was synthesized starting from 1a (36.2 mg, 201 μmol, 1.0 equiv) and thioxanthone 5 (4.34 mg, 20.4 μmol, 10 mol %) over 2.5 h. Purification by flash column chromatography (SiO2, P/EtO = 1/2, K2Cr2O7) afforded the product (35.1 mg, 181 μmol, 90%) as a colorless solid. Rf = 0.04 [KMnO4].

(3R,5aS,7aSR)-3,3a-Dimethylhexahydro-7H-3,7,3a-methano-benzofuran-7-one (8c). According to general procedure 5, compound 8c was synthesized starting from 1c (36.2 mg, 201 μmol, 1.0 equiv) and thioxanthone 5 (4.34 mg, 20.4 μmol, 10 mol %) over 2.5 h. Purification by flash column chromatography (SiO2, P/EtO = 1/2, K2Cr2O7) afforded the product (35.1 mg, 181 μmol, 90%) as a colorless solid. Rf = 0.04 [KMnO4].
(E/Z)-2-(But-2-en-1-yloxy)clohex-2-ene-1-one (E-10/Z-10). According to general procedure 1, compound E-10/Z-10 was synthesized from 4a (1.00 g, 8.92 mmol, 1.0 equiv), crotyl alcohol (E/Z = 1/1) (3.00 mL, 2.55, 35.4 mmol, 4.0 equiv), and p-TsOH·H₂O (5.17 mg, 272 μmol, 0.3% mol). Purification by flash column chromatography (SiO₂, P/Et₂O = 3/1, UV) afforded the product (150 mg, 807 μmol, 38%% as colorless oil. TLC (P/Et₂O = 3/1): Rf = 0.14 [UV, KMnO₄]. ¹H NMR (400 MHz, CDCl₃, 300 K): δ 1.72 (dd, J = 6.3 Hz, J = 1.1 Hz, 3H), 1.96 (virk. quint., J = 6.2 Hz, 2H), 2.41 (virt. td., J = 5.9 Hz, J = 4.6 Hz, 2H), 2.50 (dd, J = 7.4, 6.0 Hz, 2H), 4.20 (dd, J = 6.3 Hz, 2H), 5.62–5.71 (m, 1H), 5.71–5.83 (m, 1H), 5.88 (t, J = 4.6 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃, 300 K): δ 17.9 (q), 23.1 (t), 24.7 (t), 39.0 (t), 68.6 (t), 118.1 (d), 125.9 (d), 130.9 (d), 150.6 (s), 194.5 (s). IR (ATR) = 2939 (w), 1686 (vs), 1622 (m), 1439 (w), 1365 (w), 1259 (m), 1185 (s), 1149 (v), 1006 (m), 965 (s), 872 (w). MS (EI, 70 eV) m/z (ν[%]): 166 (21), 112 (100), 95 (6), 84 (32). HRMS (EI) m/z: [M⁺] calcd for C₄H₈O₂, 166.0989; found: 166.0988, [M⁺] calcd for C₁₃H₁₄O₂, 167.1022; found, 167.1025. UV/vis (CHCl₃, ε = 0.5 mm): λ = 260 nm (ε = 4882 cm⁻¹ M⁻¹).

(Z)-2-(Pent-2-en-1-yloxy)clohex-2-ene-1-one (Z-12). According to general procedure 2, compound Z-12 was synthesized starting from 4a (520 mg, 4.64 mmol, 1.0 equiv), (Z)-1-bromopent-2-ene (830 mg, 5.57 mmol, 1.2 equiv) and K₂CO₃ (0.770 mg, 5.57 mmol, 1.2 equiv). Purification by flash column chromatography (SiO₂, P/Et₂O = 3/1, H/EtOAc = 2/1 → 3/0 (1/0) UV) afforded the product (133 mg, 737 μmol, 17%) as colorless oil. TLC (P/Et₂O = 3/1): Rf = 0.19 [UV, KMnO₄]. ¹H NMR (500 MHz, CDCl₃, 300 K): δ 0.99 (t, J = 7.5 Hz, 3H), 1.89–2.03 (m, 2H), 2.03–2.15 (m, 2H), 2.42 (virt. td., J = 6.0 Hz, J = 4.6 Hz, 2H), 2.51 (dd, J = 7.5, 6.0 Hz, 2H), 4.36 (d, J = 5.1 Hz, 2H), 5.43–5.67 (m, 2H), 5.87 (t, J = 4.6 Hz, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃, 300 K): δ 14.2 (q), 21.3 (t), 21.3 (t), 24.7 (t), 39.0 (t), 63.8 (t), 118.2 (d), 124.0 (d), 135.7 (d), 150.5 (s), 194.6 (s). IR (ATR) = 2933 (w), 1662 (m), 1622 (m), 1457 (w), 1374 (w), 1259 (m), 1149 (m), 1149 (m), 1135 (s), 1007 (m), 873 (s) [M⁺] calcd for Z-10, 70 eV m/z (%): 210 (17), 145 (58), 129 (11), 113 (100), 99 (87), 84 (40). HRMS (EI) m/z: [M⁺] calcd for C₁₃H₁₄O₂, 180.1145; found, 180.1145, [M⁺] calcd for C₁₀H₁₂O₂, 181.1178; found, 181.1183. UV/vis (CHCl₃, ε = 0.5 mm): λ = 259 nm (ε = 3754 cm⁻¹ M⁻¹).

(Z,3aS,7aS,8SR)-8-Ethylhexahydro-7H-3,7a-methano-benzofuran-7-one (13). According to general procedure 3, compound 13 was synthesized starting from E-12 (18.1 mg, 101 μmol, 1.0 equiv) and thioxanthone S (2.14 mg, 10.2 μmol, 10 mol %) over 2.5 h. Purification by flash column chromatography (SiO₂, P/Et₂O = 1/1, KMnO₄) afforded a mixture of product 13 and olefinic byproduct 14 (18.1 mg, 100 μmol, 100%, 13/14 = 82/18) as a colorless solid.

According to general procedure 4, compound 13 was synthesized starting from Z-12 (18.1 mg, 101 μmol, 1.0 equiv) and thioxanthone S (2.17 mg, 10.1 μmol, 10 mol %) over 2.5 h. Purification by flash column chromatography (SiO₂, P/Et₂O = 1/1, KMnO₄) afforded a mixture of product 13 and olefinic byproduct 14 (16.3 mg, 90.4 μmol, 90%, 13/14 = 83/17) as a colorless solid.

The product mixture (14.2 mg, 78.8 μmol) was dissolved in 500 μL of DCE and 400 μL of H₂O. Subsequently, RuCl₃·H₂O (1 small crystal, calc. 0.14 mg, 0.7 μmol, 3.5 mol % relative to byproduct) and Na₂O₂ (18.6 mg, 87.0 μmol, 4.3 equiv) were added and the reaction mixture was stirred at room temperature for 20 h. The reaction was quenched by addition of 2.0 mL of H₂O, diluted with 2.0 mL of EtO, and the layers were separated. The aqueous layer was washed with NaHCO₃ (1 × 20 mL), H₂O (1 × 20 mL) and brine (1 × 20 mL), dried over Na₂SO₄, filtered, and the solvent was removed under reduced pressure. After purification by flash column chromatography (SiO₂, P/Et₂O = 1/1, KMnO₄) the product (98.5 mg, 54.4 μmol, 69%) was obtained as a colorless solid. Mp 58–61 °C. TLC (P/Et₂O = 1/2): Rf = 0.16 [KMnO₄]. ¹H NMR (500 MHz, CDCl₃, 300 K): δ 0.79 (t, J = 7.5 Hz, 3H), 1.21–1.33 (m, 1H), 1.37–1.51 (m, 1H), 1.63–1.78 (m, 1H), 1.93 (virk. td., J = 14.2 Hz, J = 11.0 Hz, J = 3.8 Hz, 1H), 1.99–2.09 (m, 2H), 2.09–2.16 (m, 2H), 2.12 (dd, J = 11.0, 6.7 Hz, 1H), 2.31–2.43 (m, 2H), 2.71 (d, J = 2.9 Hz, 1H), 2.84 (ddd, J = 8.6, 6.0, 2.9 Hz, 3H), 3.75 (d, J = 6.5 Hz, 1H), 3.80 (d, J = 7.5 Hz, 1H). ¹³C{¹H} NMR (126 MHz, CDCl₃, 300 K): δ 11.4 (q), 17.9 (q), 24.4 (t), 27.3 (t), 40.2 (t), 43.4 (d), 52.4 (d), 52.8 (d), 67.8 (t), 88.9 (s), 204.2 (s). IR (ATR) = 2956 (m), 1713 (vs), 1462 (w), 1327 (w), 1095 (m), 1013 (w), 947 (m), 851 (s). MS (EI, 70 eV) m/z (%): 180 (8), 151 (6), 123 (7), 113 (100), 99 (9), 95 (12), 84 (22).
HRMS (EI) m/z: [M]+ calc'd for C_{18}H_{24}O_{4}, 304.1669; found, 304.1674, [M]+ calcd for C_{17}H_{18}O_{4}.

(3R,3aR,7aR)-3-(prop-1-en-2-yl)-hexahydrobenzofuran-7(4H)-one (16a). According to general procedure 5, compound 16a was synthesized starting from 3a (18.4 mg, 102 mol%, 1.0 equiv) and thioxanthone 5 (2.21 mg, 10.4 mol%) over 4.5 h. Purification by flash column chromatography (SiO_{2}, P/Et_{2}O = 1/2, KMnO_{4}) afforded the product (11.9 mg, 66.0 mol%, 65%, dr. >95/5) as a colorless solid. Mp > 220 °C. TLC (P/Et_{2}O = 3/1): R_{f} = 0.47 [KMnO_{4}].

HRMS (EI) m/z: [M]+ calc'd for C_{18}H_{24}O_{4}, 304.1674; found, 304.1669.

(3R,3aR,7aR)-3a-Methyl-3-(prop-1-en-2-yl)-hexahydrobenzofuran-7(4H)-one (16b). According to general procedure 5, compound 16b was synthesized starting from 3b (19.6 mg, 101 mol%, 1.0 equiv) and thioxanthone 5 (2.16 mg, 10.2 mol%) over 14 h. Purification by flash column chromatography (SiO_{2}, P/Et_{2}O = 1/2, KMnO_{4}) afforded the product (16.3 mg, 86%, d.r. >95/5) as a colorless solid. Mp 95 °C.

HRMS (EI) m/z: [M]+ calc'd for C_{17}H_{18}O_{4}, 304.1669; found, 304.1674.

(3R,3aR,7aR)-5,5-Dimethyl-3-(prop-1-en-2-yl)-hexahydrobenzofuran-7(4H)-one (16c). According to general procedure 5, compound 16c was synthesized starting from 3c (24.8 mg, 120 mol%, 1.0 equiv) and thioxanthone 5 (2.57 mg, 12.1 mol%) over 1.5 h. Purification by flash column chromatography (SiO_{2}, P/Et_{2}O = 1/2, KMnO_{4}) afforded the product (21.8 mg, 101 mol%, 86%, dr. >95/5) as a colorless solid. Mp 95–101 °C. TLC (P/Et_{2}O = 3/1): R_{f} = 0.09 [KMnO_{4}].

HRMS (EI) m/z: [M]+ calc'd for C_{18}H_{26}O_{4}, 306.1723; found, 306.1722.

(3R,3aR,7aR)-3a,4a,9a,10a-Tetramethyl-6H,7H-cyclopenta[1,4]cyclobuta[1,2-f][1,5]dioxocine-1,7-dione (19). According to general procedure 5, compound 19 was synthesized starting from 2f (66.9 mg, 405 mol%, 1.0 equiv) and thioxanthone 5 (8.50 mg, 40.0 mol%) over 3 h. Purification by flash column chromatography (SiO_{2}, P/Et_{2}O = 1/1, KMnO_{4}) afforded the product (11.3 mg, 34.0 mol%, 17%) as a colorless solid. Mp 50–55 °C. TLC (P/Et_{2}O = 3/1): R_{f} = 0.44 [KMnO_{4}].

HRMS (EI) m/z: [M]+ calc'd for C_{18}H_{26}O_{4}, 306.1723; found, 306.1722.

(3R,3aR,7aR)-3a,4a,9a,10a-Tetramethyl-6H,7H-cyclopenta[1,4]cyclobuta[1,2-f][1,5]dioxocine-1,7-dione (20). According to general procedure 5, compound 20 was synthesized starting from 2f (66.9 mg, 405 mol%, 1.0 equiv) and thioxanthone 5 (8.50 mg, 40.0 mol%) over 3 h. Purification by flash column chromatography (SiO_{2}, P/Et_{2}O = 1/1, KMnO_{4}) afforded the product (17.3 mg, 80.0 mol%) as a colorless solid. Mp 25–30 °C. TLC (P/Et_{2}O = 3/1): R_{f} = 0.12 [KMnO_{4}].

HRMS (EI) m/z: [M]+ calc'd for C_{18}H_{26}O_{4}, 306.1723; found, 306.1722.
IR (ATR) ν: 2957 (m), 1742 (vs), 1540 (s), 1450 (w), 1243 (m), 1138 (s), 1043 (w), 976 (w), 902 (w). MS (EI, 70 eV) calcd for C20H28O4, 332.1982; found, 332.1983.

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