DOI: 10.1002/ejoc.201100245

Intramolecular Butenolide Allene Photocycloadditions and Ensuing Retro-Ene Reactions of Some Photoadducts

Ginger Lutteke,[a] Roel A. Kleinnijenhuis,[a] Ivo Jacobs,[a] Pauli J. Wrigstedt,[a] Ana C. A. Correia,[a] Rowan Nieuwenhuizen,[a] B. T. Buu Hue,[a] Kees Goubitz,[b] René Peschar,[b] Jan H. van Maarseveen,[a] and Henk Hiemstra*[a]

Keywords: Photochemistry / Cycloaddition / Small ring systems / Cyclobutane / Silver-mediated allylation / Retro-ene reaction / Solanoeclepin A

This report describes intramolecular [2+2] photocycloadditions of several butenolides with an allenylmethyl substituent at the 5-position. These photosubstrates were prepared from 2-(silyloxy)furans through silver-mediated reactions with allenylmethyl bromides. Two cases were studied where the lactone was replaced by an *N*-Boc-lactam. Irradiations of the photosubstrates were carried out with 300 nm UV-light in acetonitrile/acetone mixtures. Crossed cycloadducts were produced in good yields via cycloaddition of the heterocyclic double bond with the allene internal double bond. The products were γ-lactones (γ-lactams) containing the strained 5-methylenebicyclo[2.1.1]hexane skeleton. In some cases the products were unstable due to remarkably facile retro-ene reactions (1,5-hydrogen shifts) leading to unique α,β-unsaturated γ-lactone derivatives. These reactions occurred only with well-oriented C–H bonds so that strain-releasing four-membered ring opening could take place. This retro-ene reaction was studied in detail for more highly substituted derivatives in order to establish its relevance in connection with the instability of the natural terpenoid solanoeclepin A, the hatching agent of potato cyst nematodes. To this end, the methylenecyclobutane moiety in one of the cycloadducts was converted into a bicyclo[2.1.1]hexan-5-one (cyclobutanone) substructure.

Introduction

The intramolecular [2+2] photocycloaddion has been frequently used as a key step in the construction of cyclobutane-containing natural products.[1] In connection with our research toward a total synthesis of solanoeclepin A (**1**), the hatching agent of potato cyst nematodes (Figure 1), the butenolide allene [2+2] photocycloaddition was of special interest to us. For the construction of the tricyclic core of the natural product we designed a strategy based on this process.[2]

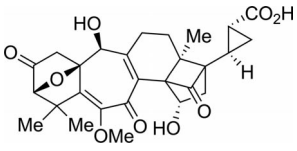
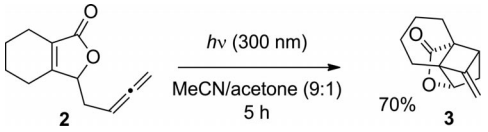


Figure 1. Structure of solanoeclepin A (**1**).

Our strategy was first tested on substrate **2** (Scheme 1). When we began our study such an intramolecular allene butenolide photocycloaddition in which the allene and the butenolide double bond are connected by a two-atom tether appeared to be unknown in the literature. We were therefore pleased to observe a smooth acetone-sensitized photocycloaddition of **2** in the desired regiochemical sense to give the tetracyclic product **3** containing the desired carbocyclic core of **1** in 70% yield. Apparently, only the allene internal double bond reacted and the cycloaddition took place in the crossed fashion.[2]

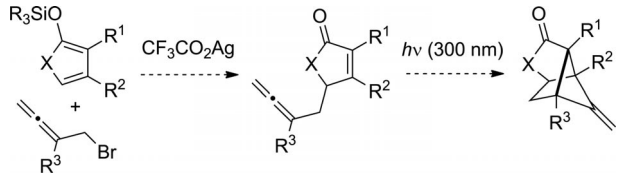


Scheme 1. The model intramolecular butenolide allene photocycloaddition.

The efficiency of this reaction and the relevance of the product structure stimulated us to study this type of intramolecular [2+2] photocycloaddition in more detail by varying the substitution pattern of the butenolide (R^1 and R^2) and the allene (R^3) (Scheme 2). Such variations in substituents can have a significant effect on the course of the [2+2] photocycloaddition, as was observed in a previous study.[2a]

[a] Laboratory of Organic Chemistry, Van 't Hoff Institute for Molecular Sciences, Faculty of Science, University of Amsterdam,
Science Park 904, 1098 XH Amsterdam, The Netherlands
Fax: +31-20-5255604
E-mail: h.hiemstra@uva.nl
[b] Laboratory of Crystallography, Van 't Hoff Institute for Molecular Sciences,
Science Park 904, 1098 XH Amsterdam, The Netherlands

After the cycloaddition these substituents end up at bridgehead carbon atoms making their introduction at a later stage virtually impossible.

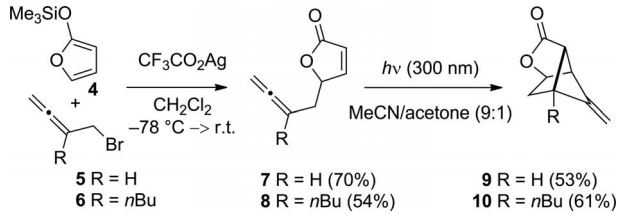


Scheme 2. General synthetic approach to the photolysis products.

We herewith report the syntheses of these photosubstrates (X = O) by using a silver-mediated coupling procedure of 2-(silyloxy)furan derivatives with the appropriate allenic bromide (Scheme 2). For the synthesis of the nitrogen analogues (X = *N*-Boc) a similar coupling of *N*-Boc-2-(silyloxy)pyrrole was used. Such silver-mediated alkylations of silyl dienol ethers were pioneered by Jefford and coworkers [3] and were first applied for the introduction of allenic substituents by us.[2a] The photosubstrates were then subjected to irradiation with 300 nm UV light providing interesting cyclic structures, some of which appeared to be susceptible to remarkably facile retro-ene reactions. The relevance of this rearrangement reaction in connection with the thermal instability of the natural product **1** itself will be discussed.

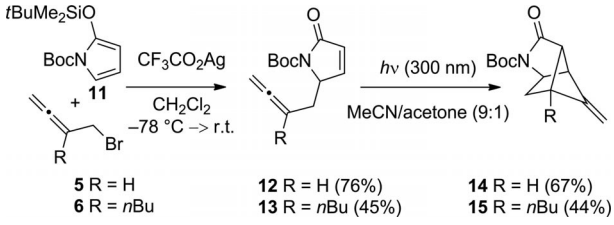
Results and Discussion

We began our studies with the parent commercially available 2-(trimethylsilyloxy)furan (**4**) as coupling partner for two allenic bromides, namely unsubstituted 2,3-butadienyl bromide **5**[4] and its 2-butyl analogue **6**, both prepared from the corresponding alcohols.[5] The silver-mediated couplings went in moderate yields to provide the photosubstrates **7** and **8**, respectively (see Scheme 3). We were pleased to find that **7** gave smooth photocycloaddition using similar conditions as for **2** requiring only 40 min of irradiation. After purification cycloadduct **9** was obtained in 53% yield. The butyl analogue **8** gave full conversion after 1 h of irradiation according to TLC. Purification provided cycloadduct **10** in 61% yield. The structures of **9** and **10** were assigned by comparison of their NMR spectra with those of **3**. Most diagnostic are the methylene protons in the ^{1}H NMR spectra as two singlets between 4.60 and 4.55 ppm and the corresponding carbon signals at ca. 150 and 94 ppm in the ^{13}C NMR spectra.



Scheme 3. The parent 2-(silyloxy)furan **4** as starting material.

The synthesis of the lactam analogues of **7** and **8** commenced with the synthesis of **11** according to a literature procedure.[6] Silver-mediated coupling with allenic bromides **5** and **6** gave the photosubstrates **12** and **13** in acceptable yields (see Scheme 4).



Scheme 4. The *N*-Boc-2-(silyloxy)pyrrole **11** as starting material.

Irradiation of **12** for 50 min resulted in complete consumption of the starting material according to TLC. Purification gave a single crystalline product in 67% yield. Recrystallization from *n*-pentane afforded crystals (m.p. 61–62 °C) suitable for X-ray analysis, which unambiguously confirmed the formation of the crossed cycloadduct **14** (Figure 2). The *n*-butyl-substituted photosubstrate **13** also participated uneventfully in the [2+2] photocycloaddition to provide **15** in 44% yield after 45 min of irradiation. Related cycloadditions of allyl-substituted pyrrol-2-ones were recently reported by Wrobel and Margaretha.[7]

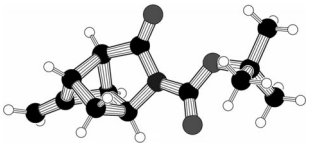
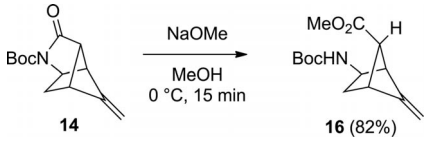


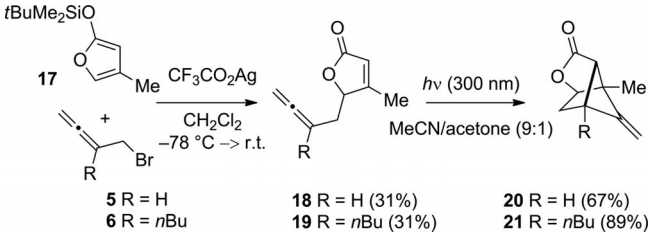
Figure 2. X-ray crystal structure of photoadduct **14**.

The lactam ring of **14** was readily opened by treatment with sodium methoxide in methanol at 0 °C for 15 min which furnished **16** in 82% yield (Scheme 5). The strained bicyclo[2.1.1]hexane skeleton of **16** has aroused considerable interest as template for mechanistic studies[8] and as backbone for novel glutamate receptor agonists.[9]



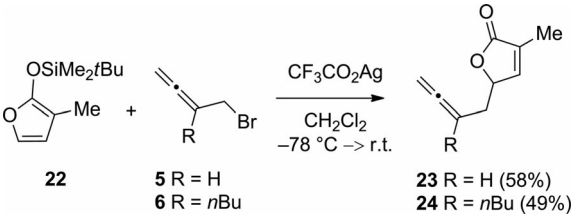
Scheme 5. Ring opening of the lactam.

Continuing our investigations we directed our attention to methyl-substituted butenolides. Coupling of the allenic bromides **5** and **6** with (silyloxy)furan **17**[10] gave the expected substitution products **18** and **19** in ca. 30% yield, apparently reflecting a steric effect of the methyl group (Scheme 6). Irradiation of these photosubstrates proceeded smoothly to give the expected cycloadducts **20** and **21** in 67% and 89% yield, respectively.



Scheme 6. 4-Methyl-2-(silyloxy)furan **17** as starting material.

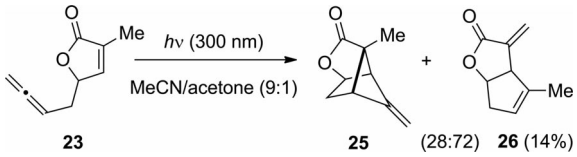
The silver-mediated coupling of (silyloxy)furan **22**[10] with allenic bromides **5** and **6** provided the desired photosubstrates **23** in 58% and **24** in 49% yield (Scheme 7).



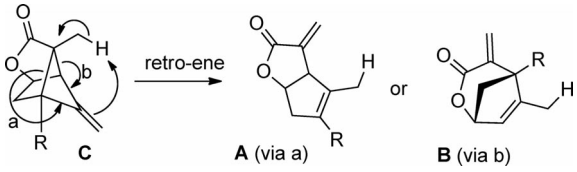
Scheme 7. 3-Methyl-2-(silyloxy)furan **22** as starting material.

When photosubstrate **23** was irradiated at 300 nm under the usual conditions, two products were formed in a ratio of 72:28 according to ^{1}H NMR (Scheme 8). Both the minor (**25**) and the major product (**26**) showed exocyclic methylene hydrogens as sharp singlets at δ = 4.73 and 4.68 ppm for the minor product and as doublets (J = 2 Hz) at δ = 6.26 and 5.69 ppm for the major product. These latter chemical shift values of the major product were at unusually low field compared to the olefinic data of the previous photoadducts. Furthermore, this major product showed another olefinic hydrogen as a broad signal at δ = 5.39 ppm, thereby ruling out the formation of the regioisomeric straight cycloadduct.[2] On the basis of ^{1}H NMR spectroscopic data it was concluded that the minor product was the expected photoadduct **25**. Chromatographic separation of the mixture failed. The major product appeared to be present in all chromatographic fractions, which indicated that the minor **25** was unstable and slowly turned into the major product. This latter product could be eventually obtained pure in 14% yield. After extensive NMR analysis the α-methylenelactone structure **26** was assigned to this product. The transformation of **25** into **26** can be viewed as an intramolecular thermal retro-ene reaction (see Scheme 8).[11] This process is shown in more detail in Scheme 9 and is in essence a 1,5-hydrogen shift of a 3-methyl-1-methylenecyclobutane moiety with relief of ring strain as a driving force. As indicated there are two possible products **A** and **B** depending on which allylic bond is cleaved. The results with **24** give conclusive evidence on this issue (vide infra).

The irradiation of **24** also resulted in the formation of two products in a ratio of 66:34 as was determined by ^{1}H NMR (Scheme 10). However, in this case the major product was the normal cycloadduct **27** indicating a slower retro-

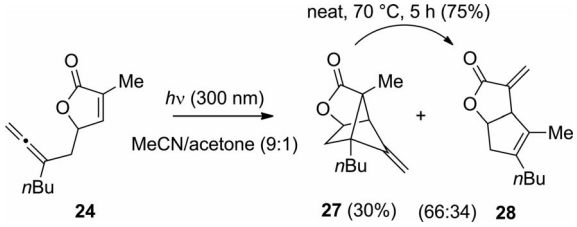


Scheme 8. Photochemistry of **23**.



Scheme 9. The two possible modes of the retro-ene reaction.

ene process. The chromatographic separation of this mixture was also tedious, but **27** could be eventually isolated in 30% yield.



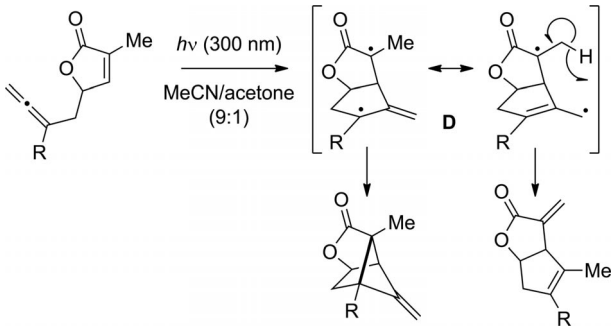
Scheme 10. Photochemistry of **24**.

With the pure cycloadduct **27** in hand the anticipated retro-ene process could be investigated in more detail. When **27** was heated as a neat sample for 5 h at 70 °C under vacuum a smooth and complete conversion to **28** was observed. Noteworthy are the mild conditions at which this retro-ene reaction occurs. Usually these 1,5-hydrogen shifts require high temperatures.[11] It was clear that the retro-ene reaction involves cleavage according to a (see **C** in Scheme 9), because product **27** showed only two alkene hydrogen signals in the ^{1}H NMR (6.21 and 5.65 ppm), indicating that the endocyclic alkene is tetrasubstituted.

The question remains how **26** and **28** are formed in the photoreaction. It is unlikely that they only arise via thermal 1,5-hydrogen shift from the [2+2]-cycloaddition products, because the temperature of the photoreaction is too low (< 45 °C). It is probable that the allylic biradical intermediate **D** can ondergo both direct radical coupling to the cyclobutane and hydrogen abstraction (Scheme 11).

The α-methylene-γ-butyrolactone moiety in the formal retro-ene products **26** and **28** is a motif that is encountered in numerous terpenoid natural products of which several display anticancer and antiviral activity.[12] This consecutive photocycloaddition fragmentation sequence constitutes a novel and interesting synthetic approach to this important class of compounds.[13]

The potential instability of complex cyclobutanes due to a remarkably facile retro-ene type 1,5-hydrogen shift could be pertinent to the chemical properties of solanoeclepin A (**1**). It is known that **1** decomposes at a temperature above

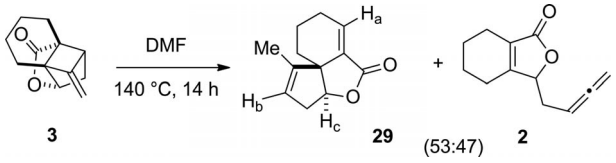


Scheme 11. Possible mechanisms of the photochemical events.

35 °C. However, it not clear which domain of the molecule is responsible for this instability.[14] Thus, the thermal sensitivity of **3** could provide some insight whether the decomposition pathway of the natural product has a bearing on such a retro-ene type rearrangement.

Therefore, the photochemical synthesis of **3** was repeated and the crude reaction mixture was carefully analyzed with ^{1}H NMR to make sure that the rearranged product had not escaped identification during the previous study.[2b] In the event byproducts could not be detected indicating that **3** was considerably less prone to rearrange than **23** or **24**. Presumably this difference is a reflection of the degree of conformational change required for the rearrangement to occur.

This became evident when we heated a sample of **3** in [D$_6$]DMSO and found that the fragmentation indeed proceeds on prolonged heating at 140 °C. The formation of the novel tricyclic product **29** was clear from the ^{1}H NMR of the crude reaction mixture showing a characteristic triplet at δ = 6.99 ppm (H$_a$), a broad signal at δ = 5.43 ppm (H$_b$) and a sharp doublet at δ = 4.56 ppm (H$_c$). In addition to **29** the allene **2** was formed in almost equal amount, which is the product of a formal retro-[2+2]-cycloaddition (Scheme 12).



Scheme 12. Thermolysis of **3**.

The use of other solvents such as DMF and xylenes did not greatly affect the ratio of **29** and **2**, but the reaction in DMF gave fewer side products and was therefore the solvent of choice for a reaction on a preparative scale (Scheme 12). After 14 h at 140 °C full conversion of the starting material was observed according to TLC. However, the separation of **29** and **2** using flash chromatography failed. Most gratifyingly, **29** could be obtained in pure form by crystallization of the combined chromatographic fractions containing both **29** and **2**. Recrystallization from hexanes provided suitable crystals (m.p. 69–71 °C) for X-ray analysis, which unambiguously confirmed the proposed structure of **29** (Figure 3).

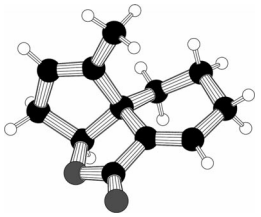
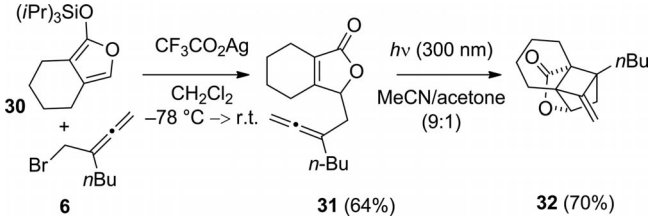


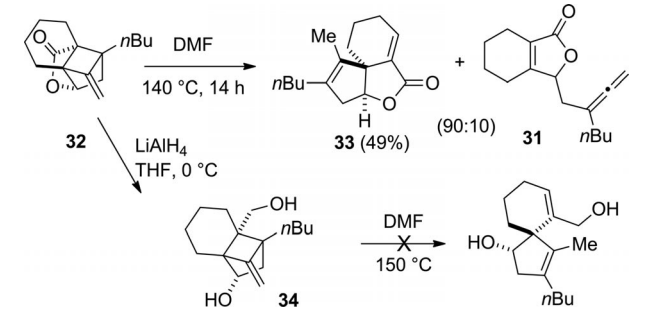
Figure 3. X-ray crystal structure of retro-ene product **29**.

The *n*-butyl analogue of **3** was constructed in a straightforward fashion by first coupling of allenyl bromide **6** and 2-(silyloxy)furan **30** to give **31** in 64% yield. A smooth cycloaddition was observed upon irradiation of **31** at 300 nm for 1.5 h and a single product was detected using ^{1}H NMR, which was isolated in 70% yield (Scheme 13).



Scheme 13. Synthesis and photolysis of **31**.

As for **3**, on heating a solution of **32** in DMF at 140 °C for 14 h the rearranged product **33** was obtained along with a small amount of **31** in a ratio of 90:10 (Scheme 14). The separation of these two products using standard flash chromatography was again difficult. However, **33** could be obtained in pure form in 49% yield via recrystallization of the combined chromatographic fractions containing both **31** and **33**. The structure of **33** was assigned by comparison of its ^{1}H NMR spectroscopic data with those of **29**.



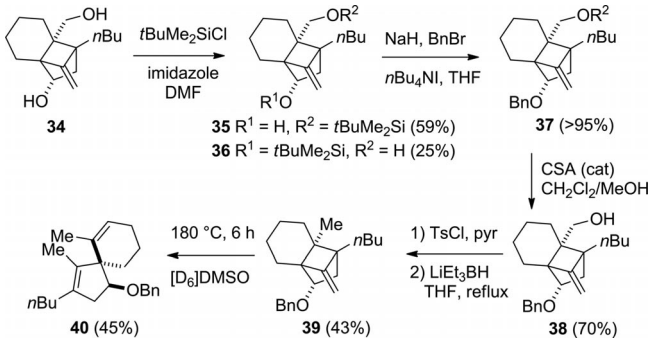
Scheme 14. Thermolysis and reduction of **32**.

At this stage it is interesting to return to the thermal sensitivity of solanoeclepin A (**1**). Structural features of **1** are the secondary hydroxy group and the bridgehead methyl group, which are positioned on the cyclopentane ring of the tricyclic core of the natural product. These groups are being masked in the model substrates **3** and **32** as lactone rings. From molecular models it is clear that this difference in backbone structure has a significant effect on the conformation and therefore on the spatial orientation of the two reacting groups in the retro-ene rearrangement. Therefore, **32** was fully reduced to diol **34** by treatment with LiAlH$_4$

and then heated in DMF. Interestingly this diol did not give a clean retro-ene reaction. On prolonged heating at 150 °C decomposition products were observed in ^{1}H NMR, which did not reveal the typical signals of the spiro compound as shown in Scheme 14.

This finding suggests that the thermal 1,5-hydrogen shift is facilitated through the stereoelectronic effects of the lactone ring. As this structural motif is not present in the natural product, we reasoned that it is quite unlikely that the thermal instability of **1** can be ascribed to the retro-ene reaction. To get experimental proof for this assumption we set out to convert **34** into a compound, which is more natural product like by conversion of the primary alcohol into a methyl.

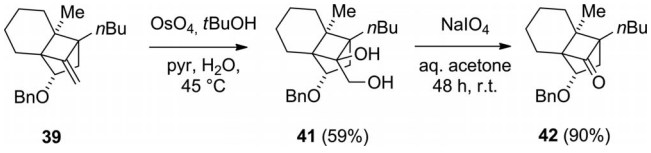
Silylation of **34** using TBSCl in DMF resulted in the formation of two mono-protected alcohols **35** and **36**, which were isolated in 59% and 25% yield in favor of the desired regioisomer (Scheme 15). After some experimentation it became clear that the selectivity could not be increased even using protocols for selective protection of primary over secondary alcohols (TBSCl, DMAP). The isomers could be readily separated using flash chromatography and the undesired isomer could be converted back into **34** upon desilylation (TBAF, THF) to ensure material throughput. The alcohol **38** was obtained through protection of the remaining hydroxy group in **35** (BnBr, NaH, THF) followed by desilylation (CSA, MeOH). Conversion of the hydroxy group into a tosylate and subsequent reductive removal using lithium triethylborohydride gave the bridgehead methyl group and completed the synthesis of **39**. With this substrate in hand the retro-ene reaction could be investigated. Heating a sample in [D$_6$]DMSO showed an increased stability compared to **34**, because at a temperature of 150 °C no decomposition was observed. However, a further increase of the temperature to 180 °C did cause a slow conversion into the retro-ene rearrangement product **40**. A complete transformation was observed after 6 h of heating and **40** could be isolated in 45% yield. This example shows that the lactone ring is not essential for the retro-ene reaction and that this still might be possible in the natural product.



Scheme 15. Synthesis and thermolysis of **39**.

The temperatures at which the rearrangements of the substrates occur are still much higher than the 35 °C at which the natural product decomposes. An obvious reason might be that the natural product is a cyclobutanone instead of a methylenecyclobutane. The ketone oxygen could well speed up the retro-ene reaction. Precedent for an easier retro-ene process in the case of cyclopropyl ketones compared with the methylene analogues is available.[11] We could only find one single example in the literature of a retro-ene reaction of a highly strained 3-alkylcyclobutanone in a fashion as expected here.[15] The most usual way in which cyclobutanones decompose at high temperature is via a ketene olefin [2+2]-cycloreversion.[16]

Thus, we decided to transform **39** into the cyclobutanone **42** according to our previously published method. (Scheme 16)[2b] Thus, dihydroxylation of the double bond using OsO_4 followed by cleavage of the vicinal diol gave the desired ketone **42**. The heating a sample of **42** in [D$_6$]-DMSO was carefully studied by ^{1}H NMR spectroscopy. The temperature was slowly raised. Already at 110 °C a rather quick decomposition of **42** into several products was observed. Unfortunately, attempts to purify the mixture failed and none of the products could be obtained in pure form. Despite the purification problems, the discovery that the cyclobutanone analogue of **39** has a lower thermal stability provides some experimental support that the cyclobutanone may play a role in the decomposition pathway of **1**.



Scheme 16. Synthesis of cyclobutanone **42**.

Conclusions

Silver-mediated reactions of 2-(silyloxy)furans with allenylmethyl bromides proceeded well to produce several butenolides with an allenylmethyl substituent at the 5-position. These products were excellent substrates for intramolecular [2+2] photocycloaddition processes (300 nm, acetonitrile/acetone, 9:1), giving γ-lactones containing the strained 5-methylenebicyclo[2.1.1]hexane skeleton. Some of the products reacted further via a retro-ene reaction (a 1,5-hydrogen shift) to furnish unique α,β-unsaturated lactone derivatives. All of these reactions are important in conjunction with our synthetic approach toward solanoeclepin A, the hatching agent of potato cyst nematodes. The instability of this natural product at temperatures above 35 °C might be related to the inherent vulnerability of 3-alkylcyclobutanones to retro-ene decomposition.

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 CH_2Cl_2 and acetonitrile were distilled from CaH_2. 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 ^{13}C. Unless otherwise stated, $CDCl_3$ 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 wavenumbers ($\tilde{\nu}$) 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.

3-(Bromomethyl)hepta-1,2-diene (6): To a solution of 2-vinylidenehexan-1-ol[5] (5.30 g, 42.0 mmol) in CH_2Cl_2 (50 mL) at 0 °C was added methanesulfonyl chloride (4.9 mL, 7.29 g, 50.4 mmol). Then triethylamine (6.8 mL, 5.10 g, 50.4 mmol) was added dropwise. The reaction was stirred for 1 h. The mixture was diluted with CH_2Cl_2 (50 mL), washed with water (3×), dried with $MgSO_4$ and concentrated in vacuo. ^1H NMR: δ = 4.91–4.87 (m, 2 H, C=CH_2), 4.71–4.69 (m, 2 H, CH_2OMs), 3.00 (s, 3 H, SO_2CH_3), 2.11–2.05 (m, 2 H, CH_2 *n*Bu), 1.51–1.40 (m, 2 H, CH_2 *n*Bu), 1.40–1.31 (m, 2 H, CH_2 *n*Bu), 0.90 (t, J = 7.3 Hz, 3 H, CH_3 *n*Bu). This crude mesylate was used in the next reaction without further purification. It was dissolved in 20 mL of acetone and then added dropwise to a suspension of LiBr (14.59 g, 168 mmol) in acetone (80 mL) at 0 °C. The reaction was stirred for 1 h. The mixture was filtered and concentrated in vacuo. Purification of the residue by column chromatography (hexanes) afforded **6** (6.41 g, 34.0 mmol, 81% over two steps) as a colorless oil. ^1H NMR: δ = 4.79 (s, 2 H, C=CH_2), 4.02 (s, 2 H, CH_2Br), 2.12 (m, 2 H, CH_2 *n*Bu), 1.46–1.33 (m, 4 H, 2×CH_2 *n*Bu), 0.92 (t, J = 7 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 206.9 (=C=), 101.2 (>C=), 76.5 (=CH_2), 46.9 (CH_2Br), 35.6 (CH_2), 29.1 (CH_2), 22.1 (CH_2), 13.7 (CH_3) ppm. IR: $\tilde{\nu}$ = 2958, 1953 cm^{-1}.

General Procedure for the Preparation of the Photosubstrates via Silver-Mediated Coupling: To a well stirred suspension of dried powdered 4 Å molecular sieves (same amount in weight as the allenic bromide) and silver trifluoroacetate (1.2 equiv.) in CH_2Cl_2 (0.5 M) at –78 °C was added a solution of the allenic bromide (1.2 equiv.) in CH_2Cl_2 (0.4 M). After 5 min, a solution of 2-(silyloxy)furan or 2-(silyloxy)pyrrole (1 equiv.) in CH_2Cl_2 (0.4 M) was added. The mixture was well stirred and warmed to room temperature overnight followed by filtration through Celite. The solvent was removed in vacuo and the residue purified using flash chromatography.

5-(Buta-2,3-dien-1-yl)furan-2(5*H*)-one (7): Prepared according to the general procedure from 2-(trimethylsiloxy)furan (**4**) (0.75 mL, 4.48 mmol). Purification of the residue by chromatography (hexanes/EtOAc, 2:1) afforded **7** as a light yellow oil (429 mg, 70%). ^1H NMR: δ = 7.50 (dd, J = 5.7, 1.4 Hz, 1 H, 4-H), 6.13–6.11 (m, 1 H, 3-H), 5.11–5.03 (m, 2 H, 5-H, CH=), 4.79–4.71 (m, 2 H, =CH_2), 2.51–2.40 (m, 2 H, CH_2) ppm. ^{13}C NMR: δ = 209.4 (=C=), 172.7 (C-2), 155.6 (C-4), 121.9 (C-3), 83.5 (HC=), 82.2 (C-5), 75.8 (=CH_2), 31.9 (CH_2) ppm. IR (neat): $\tilde{\nu}$ = 3026, 2924, 1957, 1769, 1602 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_8H_9O_2$ 137.0603; found 137.0604 $[M + H]^+$.

5-(2-Vinylidenehexyl)furan-2(5*H*)-one (8): Prepared according to the general procedure from 2-(trimethylsiloxy)furan (**4**) (0.75 mL, 4.48 mmol). Purification of the residue by chromatography (hexanes/EtOAc, 4:1) afforded **8** as a colorless oil (597 mg, 54%). ^1H NMR: δ = 7.45 (d, J = 5.0 Hz, 1 H, 4-H), 5.93–5.91 (m, 1 H, 3-H), 5.02–4.99 (m, 1 H, 5-H), 4.62–4.60 (m, 2 H, =CH_2), 2.22–2.12 (m, 1 H, *H*-CH), 2.10–2.08 (m, 1 H, HC-*H*), 1.80–1.75 (m, 2 H, CH_2 *n*Bu), 1.25–1.14 (m, 4 H, 2×CH_2 *n*Bu), 0.72 (t, J = 7.1 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 205.6 (=C=), 172.5 (C-2), 156.4 (C-4), 121.0 (C-3), 97.9 (>C=), 81.7 (C-5), 76.8 (=CH_2), 35.3 (CH_2), 31.8 (CH_2 *n*Bu), 29.2 (CH_2 *n*Bu), 21.9 (CH_2 *n*Bu), 13.6 (CH_3) ppm. IR (neat): $\tilde{\nu}$ = 1975, 1748 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{12}H_{17}O_2$ 193.1223; found 193.1229 $[M + H]^+$.

***tert*-Butyl 2-(Buta-2,3-dien-1-yl)-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (12):** Prepared according to the general procedure from (silyloxy)pyrrole **11** (1.0 g, 3.4 mmol).[6] Purification of the residue by chromatography (hexanes/EtOAc, 1:1) provided **12** as an orange solid (600 mg, 67%); m.p. 66–68 °C. ^1H NMR: δ = 7.15–7.13 (m, 1 H, 4-H), 6.09–6.07 (m, 1 H, 3-H), 4.90–4.85 (m, 1 H, HC=), 4.69–4.63 (m, 3 H, 5-H, =CH_2), 2.71–2.66 (m, 1 H, *H*-CH), 2.45–2.40 (m, 1 H, HC-*H*), 1.52 (s, 9 H, Boc) ppm. ^{13}C NMR: δ = 209.5 (=C=), 169.1 (C-2), 149.6 (C-4), 149.1 (C=O, Boc), 126.9 (C-3), 83.1 (HC=), 82.9 (C_q Boc), 75.3 (=CH_2), 61.6 (C-5), 30.4 (CH_2), 27.9 (CH_3 Boc) ppm. IR: $\tilde{\nu}$ = 2956, 1956, 1774, 1731 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{13}H_{17}NO_3$ 236.1287; found 236.1290 $[M + H]^+$.

***tert*-Butyl 2-Oxo-5-(2-vinylidenehexyl)-2,5-dihydro-1*H*-pyrrole-1-carboxylate (13):** Prepared according to the general procedure from (silyloxy)pyrrole **11**[6] (500 mg, 1.7 mmol). Purification of the residue by chromatography (hexanes/EtOAc, 1:1) provided **13** as a yellow oil (220 mg, 45%). ^1H NMR: δ = 7.20 (dd, J = 6.1, 2.0 Hz, 1 H, 4-H), 6.00 (dd, J = 6.1, 1.4 Hz, 1 H, 3-H), 4.70–4.67 (m, 2 H, =CH_2), 4.64–4.61 (m, 1 H, 5-H) 2.78–2.74 (m, 1 H, *H*-CH), 2.06–1.97 (m, 1 H, HC-*H*), 1.88–1.86 (m, 2 H, CH_2 *n*Bu), 1.53 (s, 9 H, Boc), 1.36–1.18 (m, 4 H, 2×CH_2 *n*Bu), 0.83 (t, J = 7.1 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 205.9 (=C=), 168.9 (C-2), 150.5 (C-4), 149.1 (C=O, Boc), 126.1 (C-3), 98.1 (>C=), 82.7 (C_q Boc), 76.5 (=CH_2), 61.2 (C-5), 34.4 (CH_2), 32.3 (CH_2 *n*Bu), 29.4 (CH_2 *n*Bu), 27.9 (CH_3 Boc), 22.0 (CH_2), 13.7 (CH_3) ppm. IR: $\tilde{\nu}$ = 1965, 1773, 1730 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{17}H_{25}NO_3Na$ 314.1732; found 314.1736 $[M + Na]^+$.

5-(Buta-2,3-dien-1-yl)-4-methylfuran-2(5*H*)-one (18): Prepared according to the general procedure from furan **17**[10] (1.2 g, 5.7 mmol). Purification of the residue by chromatography (hexanes/EtOAc, 4:1) provided **18** as a colorless oil (262 mg, 31%). ^1H NMR: δ = 5.79 (t, J = 1.4 Hz, 1 H, 3-H), 4.99–4.89 (m, 1 H, HC=), 4.89 (t, J = 1.0 Hz, 1 H, 5-H), 4.73–4.63 (m, 2 H, =CH_2), 2.65–2.58 (m, 1 H, *H*-CH), 2.34–2.25 (m, 1 H, HC-*H*), 2.07 (s, 3 H, CH_3) ppm. ^{13}C NMR: δ = 209.8 (=C=), 173.2 (C-2), 168.2 (C-4), 117.9 (C-3), 83.8 (HC=), 83.3 (C-5), 75.8 (=CH_2), 31.2 (CH_2), 14.2 (CH_3) ppm. IR: $\tilde{\nu}$ = 1958, 1753 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_9H_{10}O_2$ 151.0759; found 151.0578 $[M + H]^+$.

4-Methyl-5-(2-vinylidenehexyl)furan-2(5*H*)-one (19): Prepared according to the general procedure from furan **17**[10] (1.0 g, 4.7 mmol). Purification of the residue by chromatography (hexanes/EtOAc, 4:1) provided **19** as a colorless oil (305 mg, 31%). ^1H NMR: δ = 5.81 (t, J = 1.2 Hz, 1 H, 3-H), 4.99 (t, J = 5.6 Hz, 1 H, 5-H), 4.80–4.66 (m, 2 H, =CH_2), 2.50–2.42 (m, 1 H, *H*-CH), 2.25–2.17 (m, 1 H, HC-*H*), 2.08 (s, 3 H, CH_3), 2.01–1.91 (m, 2 H, CH_2 *n*Bu), 1.42–1.23 (m, 4 H, 2×CH_2 *n*Bu), 0.86 (t, J = 7.0 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 206.4 (=C=), 173.7 (C-2), 169.1 (C-4), 117.5 (C-3), 98.7 (>C=), 83.8 (C-5), 77.4 (=CH_2), 35.1 (CH_2), 32.4 (CH_2, *n*Bu), 29.8 (CH_2, *n*Bu), 22.5 (CH_2, *n*Bu), 14.5 (CH_3), 14.1 (CH_3, *n*Bu) ppm. IR: $\tilde{\nu}$ = 1957, 1745 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{13}H_{18}O_2$ 207.1385; found 207.1387 $[M + H]^+$.

5-(Buta-2,3-dien-1-yl)-3-methylfuran-2(5*H*)-one (23): Prepared according to the general procedure from **22**[10] (200 mg, 0.91 mmol). Purification of the residue by chromatography (hexanes/EtOAc,

4:1) provided **23** as a colorless oil (79 mg, 58%). ^{1}H NMR: δ = 7.08 (q, J = 1.6 Hz, 1 H, 4-H), 5.12–5.04 (m, 1 H, HC=), 5.00–4.93 (m, 1 H, C-5), 4.79–4.70 (m, 2 H, =CH_2), 2.51–2.32 (m, 2 H, CH_2), 1.91 (t, J = 1.5 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 209.7 (=C=), 174.3 (C-2), 148.4 (C-4), 130.7 (C-3), 84.1 (HC=), 80.4 (C-5), 76.0 (=CH_2), 32.6 (CH_2), 10.9 (CH_3) ppm. IR: $\tilde{\nu}$ = 1957, 1746 cm^{-1}. HR-MS: m/z calcd. for $C_9H_{11}O_2$ 151.0759; found 151.0758 [M + H]$^+$.

3-Methyl-5-(2-vinylidenehexyl)furan-2(5*H*)-one (24): Prepared according to the general procedure from furan **22**[10] (170 mg, 0.81 mmol). Purification of the residue by chromatography (hexanes/EtOAc, 4:1) provided **24** as a colorless oil (82 mg, 49%). ^{1}H NMR: δ = 7.12 (q, J = 1.6 Hz, 1 H, 4-H), 5.05–4.97 (m, 1 H, 5-H), 4.81–4.73 (m, 2 H, =CH_2), 2.48–2.38 (m, 1 H, *H*-CH), 2.21–2.12 (m, 1 H, HC-*H*), 2.00–1.93 (m, 2 H, CH_2), 1.90 (t, J = 1.6 Hz, 3 H, CH_3), 1.45–1.28 (m, 4 H, 2 × CH_2 *n*Bu), 0.88 (t, J = 7.1 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 206.1 (=C=), 174.4 (C-2), 149.0 (C-4), 130.2 (C-3), 98.7 (>C=), 79.9 (C-5), 77.3 (=CH_2), 36.2 (CH_2), 32.5 (CH_2, *n*Bu), 29.7 (CH_2, *n*Bu), 22.5 (CH_2, *n*Bu), 14.2 (CH_3, *n*Bu), 10.9 (CH_3) ppm. IR: $\tilde{\nu}$ = 1956, 1753 cm^{-1}. HR-MS: m/z calcd. for $C_{13}H_{18}O_2$: 207.1385; found 207.1387 [M + H]$^+$.

3-(2-Vinylidenehexyl)-4,5,6,7-tetrahydroisobenzofuran-1(3*H*)-one (31): Prepared according to the general procedure from furan **30**[2b] (2.13 g, 7.25 mmol). Purification of the residue by chromatography (hexanes/EtOAc, 9:1 to 8:2) gave **31** as a colorless oil (1.14 g, 64%). ^{1}H NMR: δ = 4.95–4.93 (m, 1 H, 3-H), 4.76–4.68 (m, 2 H, =CH_2), 2.44–2.37 (m, 1 H, *H*-CH), 2.28–2.19 (m, 5 H, HC-*H*, 2 × CH_2), 1.99–1.94 (m, 2 H, CH_2 *n*Bu), 1.74–1.67 (m, 4 H, 2 × CH_2), 1.41–1.29 (m, 4 H, 2 × CH_2 *n*Bu), 0.89 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 206.0 (=C=), 173.3 (C-1), 163.4 (C-9), 126.6 (C-8), 98.3 (>C=), 81.4 (C-3), 76.6 (=CH_2), 34.9 (CH_2), 32.1 (CH_2, *n*Bu), 29.4 (CH_2, *n*Bu), 23.2 (CH_2), 22.1 (CH_2, *n*Bu), 21.4 (CH_2), 21.3 (CH_2), 19.7 (CH_2), 13.7 (CH_3) ppm. IR: $\tilde{\nu}$ = 2929, 1957, 1746 cm^{-1}. HR-MS: m/z calcd. for $C_{16}H_{23}O_2$ 247.1698; found 247.1699 [M + H]$^+$.

General Procedure for the [2+2] Photocycloadditions: A solution of the photosubstrate in a mixture of acetonitrile/acetone (9:1) was degassed by bubbling argon through the solution for 30 min. The solution was kept under argon during the irradiation and the reaction vessel was air-cooled with a fan which kept the temperature below ca. 45 °C. The irradiation was continued until complete conversion of the starting material was observed with TLC. The solvent was removed in vacuo and the residue purified.

8-Methylene-4-oxatricyclo[3.3.0.0^{2,7}]octan-3-one (9): According to the general procedure a solution of **7** (93 mg, 0.68 mmol) in 25 mL acetonitrile/acetone (9:1) was irradiated for 40 min. The solvent was removed and the residue purified by chromatography (hexanes/EtOAc, 2:1) to give **9** as a light yellow oil (49 mg, 53%). ^{1}H NMR: δ = 4.98–4.97 (m, 1 H, 5-H), 4.60 (s, 1 H, =C*H*H), 4.55 (s, 1 H, =CH*H*), 3.62–3.59 (m, 1 H), 3.29–3.28 (m, 1 H), 2.97–2.96 (m, 1 H), 2.09 (dd, J = 12, 4 Hz, 1 H), 1.78 (dd, J = 12, 2 Hz, 1 H) ppm. ^{13}C NMR: δ = 173.8 (C-3), 148.7 (C-8), 94.8 (=CH_2), 78.9 (C-5), 59.0, 48.8, 46.1, 35.1 (C-6) ppm. IR: $\tilde{\nu}$ = 3100, 1766 cm^{-1}. HR-MS: m/z calcd. for $C_8H_9O_2$ 137.0597; found 137.0612 [M + H]$^+$.

7-Butyl-8-methylene-4-oxatricyclo[3.3.0.0^{2,7}]octan-3-one (10): According to the general procedure a solution of **8** (491 mg, 2.56 mmol) in 60 mL acetonitrile/acetone (9:1) was irradiated for 1 h. The solvent was removed and the residue purified by chromatography (hexanes/EtOAc, 5:1) to give **10** as a light yellow oil (300 mg, 61%). ^{1}H NMR: δ = 4.97–4.96 (m, 1 H, 5-H), 4.57 (s, 1 H, =CH*H*), 4.55 (s, 1 H, =C*H*H), 3.57 (t, J = 4.0 Hz, 1 H, 2-H), 2.74 (s, 1 H, 1-H), 2.00 (ddd, J = 11.9, 4.0, 1.4 Hz, 1 H, 6-H), 1.81–1.76 (m, 2 H, CH_2 *n*Bu), 1.69 (d, J = 11.9 Hz, 1 H, 6′-H), 1.38–1.33 (m, 4 H, 2 × CH_2 *n*Bu), 0.94 (t, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 174.3 (C-3), 152.2 (C-8), 92.7 (=CH_2), 79.8 (C-5), 59.5 (C-7), 57.1 (C-2), 51.9 (C-1), 38.3 (C-6), 28.5 (CH_2), 27.4 (CH_2), 22.9 (CH_2), 13.8 (CH_3) ppm. IR: $\tilde{\nu}$ = 1766, 1697 cm^{-1}. HR-MS: m/z calcd. for $C_{12}H_{17}O_2$ 193.1229; found 193.1229 [M + H]$^+$.

***tert*-Butyl 8-Methylene-3-oxo-4-azatricyclo[3.3.0.0^{2,7}]octane-4-carboxylate (14):** According to the general procedure a solution of **12** (104 mg, 0.44 mmol) in 30 mL acetonitrile/acetone (9:1) was irradiated for 50 min. The solvent was removed and the residue purified by chromatography (hexanes/EtOAc, 1:1) to give **14** as a white solid (70 mg, 67%); m.p. 61–62 °C. ^{1}H NMR: δ = 4.61–4.60 (m, 1 H, 5-H), 4.58 (s, 1 H, =CH*H*), 4.53 (s, 1 H, =C*H*H), 3.28–3.26 (m, 2 H, 1-H, 7-H), 2.88–2.87 (m, 1 H, 2-H), 2.12 (dd, J = 11.3, 4.5 Hz, 1 H, 6-H), 1.62 (dd, J = 11.4, 1.9 Hz, 1 H, 6′-H), 1.53 (s, 9 H, Boc) ppm. ^{13}C NMR: δ = 170.7 (C-3), 149.3 (C=O, Boc), 149.0 (C-8), 94.4 (=CH_2), 83.1 (C_q, Boc), 57.3 (C-5), 55.2 (C-2), 52.3 (C-1), 47.4 (C-7), 35.4 (C-6), 28.1 (CH_3) ppm. IR: $\tilde{\nu}$ = 1780, 1745, 1701 cm^{-1}. HR-MS: m/z calcd. for $C_{13}H_{17}NO_3$ 236.1287; found 236.1286 [M + H]$^+$. $C_{13}H_{17}NO_3$ (235.279): calcd. C 66.36, H 7.28, N 5.95; found C 66.21, H 7.16, N 5.88.

X-ray Crystal Structure Analysis of 14: $C_{13}H_{17}NO_3$, M = 235.28, T = 253 K, λ = 1.5418 Å; triclinic, $P\bar{1}$, a = 11.697(14) Å, b = 11.732(14) Å, c = 11.851(2) Å, α = 117.71(4)°, β = 114.89(4)°, γ = 91.24(12)°, V = 1257(3) Å^3, Z = 4, D_x = 1.24 g cm^{-3}, 4243 observed unique reflections, R_1 = 0.061.

CCDC-765944 contains the supplementary crystallographic data for **14**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Methyl (1*S,2*R**,4*R**,5*S**)-2-[(*tert*-Butoxycarbonyl)amino]-6-methylenebicyclo[2.1.1]hexane-5-carboxylate (16):** To a solution of **14** (50 mg, 0.17 mmol) in 1 mL MeOH was added at 0 °C a solution of 152 μL of a 2 M solution of MeONa in MeOH. The mixture was stirred for 15 min at 0 °C and quenched by the addition of brine. The resulting mixture was extracted with diethyl ether (3×) and the combined organics were washed with water and brine and dried using $MgSO_4$. The solvent was removed and the residue purified by chromatography (hexanes/EtOAc, 1:1) to give **16** as a colourless oil (38 mg, 82%). ^{1}H NMR: δ = 5.39 (br. s, 1 H, NH), 4.47 (s, 2 H, =CH_2), 4.08 (m, 1 H, 2-H), 3.69 (s, 3 H, OMe), 3.36–3.37 (m, 1 H, 1-H), 3.13–3.14 (m, 1 H, 2-H), 2.74 (m, 1 H, 5-H), 2.25.2.24 (m, 1 H, 3-H), 1.79–1.76 (m, 1 H, 3′-H), 1.45 (s, 9 H, Boc) ppm. ^{13}C NMR: δ = 172.4 (C=O ester), 155.6 (C=O Boc), 150.2 (C-6), 93.6 (=CH_2), 79.1 (C_q Boc), 55.3 (C-2), 51.7 (OMe), 49.1 (C-1), 48.8 (C-2), 44.1 (C-5), 33.0 (C-3), 28.4 (CH_3) ppm. HR-MS: m/z calcd. for $C_{14}H_{22}NO_4$ 268.1549; found 268.1550 [M + H]$^+$.

***tert*-Butyl 7-Butyl-8-methylene-3-oxo-4-azatricyclo[3.3.0.0^{2,7}]octane-4-carboxylate (15):** According to the general procedure a solution of **13** (72 mg, 0.25 mmol) in 20 mL acetonitrile/acetone (9:1) was irradiated for 45 min. The solvent was removed and the residue purified by chromatography (hexanes/EtOAc, 2:1) to give **15** as a colorless oil (31 mg, 44%). ^{1}H NMR: δ = 4.58–4.56 (m, 1 H, 5-H), 4.51 (s, 1 H, =CH*H*), 4.50 (s, 1 H, =C*H*H), 3.23–3.21 (m, 1 H, 1-H), 2.61 (s, 1 H, 2-H), 2.03–1.99 (m, 1 H, 6-H), 1.77–1.73 (m, 2 H, CH_2 *n*Bu), 1.53–1.50 [m, 10 H, $C(CH_3)_3$, 6′-H], 1.37–1.32 (m, 4 H, 2 × CH_2 *n*Bu), 0.91–0.88 (t, J = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 171.2 (C-3), 152.4 (C-8), 149.4 (C=O, Boc), 92.3 (=CH_2), 83.0 (C_q, Boc), 60.8 (C-7), 58.4 (C-5), 55.5 (C-1), 53.4 (C-2), 38.7 (C-6), 28.8 (CH_2), 28.1 (CH_2), 27.6 (CH_3, Boc), 23.1 (CH_2), 13.4 (CH_3) ppm. IR: $\tilde{\nu}$ = 1779, 1743, 1708 cm^{-1}. HR-MS: m/z calcd. for $C_{17}H_{25}NO_3$ 292.1913; found 292.1917 [M + H]$^+$.

1-Methyl-8-methylene-4-oxatricyclo[3.3.0.0^{2,7}]octan-3-one (20): According to the general procedure a solution of **18** (192 mg, 1.28 mmol) in 30 mL acetonitrile/acetone (9:1) was irradiated for 2 h. The solvent was removed and the residue purified by chromatography (*n*-pentane/Et_2O, 2:1) to give **20** as a light yellow oil (128 mg, 67%). ^{1}H NMR: δ = 4.61–4.55 (m, 2 H, =CH_2), 4.49 (s, 1 H, 5-H), 3.26 (s, 1 H, 7-H), 2.68 (t, J = 1.4 Hz, 1 H, 2-H), 2.17–2.09 (m, 1 H, 6-H), 1.77 (dd, J = 12.0, 2.4 Hz, 1 H, 6′-H), 1.33 (s, 3 H, CH_3) ppm. ^{13}C NMR: δ = 173.7 (C-3), 152.4 (C-8), 92.3 (=CH_2), 82.7 (C-5), 66.8 (C-1), 53.1 (C-2), 44.8 (C-7), 36.2 (C-6), 9.9 (CH_3) ppm. IR: $\tilde{\nu}$ = 1768 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_9H_{11}O_2$ 151.0759; found 151.0755 [M + H]$^+$.

7-Butyl-1-methyl-8-methylene-4-oxatricyclo[3.3.0.0^{2,7}]octan-3-one (21): According to the general procedure a solution of **19** (58 mg, 0.28 mmol) in 30 mL acetonitrile/acetone (9:1) was irradiated for 30 min. The solvent was removed and the residue purified by chromatography (*n*-pentane/Et_2O, 1:1) to give **21** as a light yellow oil (39 mg, 67%). ^{1}H NMR: δ = 4.50 (dd, J = 4.0, 1.4 Hz, 1 H, 5-H), 4.47 (s, 1 H, =CH*H*), 4.43 (s, 1 H, =C*H*H), 2.38 (s, 1 H, 2-H), 1.95 (ddd, J = 11.6, 3.6, 1.2 Hz, 1 H, 6-H), 1.72–1.67 (m, 2 H, CH_2 *n*Bu), 1.63 (d, J = 12.0 Hz, 1 H, 6′-H), 1.33–1.22 (m, 7 H, 2 × CH_2, CH_3), 0.85 (t, J = 6.8 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 174.2 (C-3), 156.0 (C-8), 90.5 (=CH_2), 83.7 (C-5), 64.7 (C-1), 58.3 (C-7), 56.5 (C-2), 39.8 (C-6), 28.5 (CH_2), 27.6 (CH_2), 22.9 (CH_2), 13.8 (CH_3, *n*Bu), 9.9 (CH_3) ppm. IR: $\tilde{\nu}$ = 1767 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{13}H_{19}O_2$ 207.1385; found 207.1387 [M + H]$^+$.

Irradiation of Photosubstrate 23: According to the general procedure a solution of **23** (100 mg, 0.67 mmol) in 30 mL MeCN/acetone was irradiated for 3 h at 300 nm. The solvent was removed and the residue (mixture of **25** and **26** in a ratio 28:72 according to ^{1}H NMR) was purified by chromatography (hexanes/EtOAc, 4:1) to give pure **26** as a light yellow oil (14 mg, 14%). The minor product **25** could not be obtained pure due to slow transformation into **26**. Data for 4-methyl-3-methylene-3,3a,6,6a-tetrahydro-2*H*-cyclopenta[*b*]furan-2-one (**26**): ^{1}H NMR: δ = 6.26 [d, J = 2.0 Hz, 1 H (=C*H*H)], 5.69 (d, J = 1.6 Hz, 1 H, =CH*H*), 5.39 (s, 1 H, 5-H), 5.12 (m, 1 H, 7-H), 3.77 (m, 1 H, 8-H), 2.82–2.64 (m, 2 H), 1.72 (m, 3 H) ppm. ^{13}C NMR: δ = 170.3 (C-2), 137.3 (C-4), 135.8 (C-3), 124.0 (=CH_2), 122.0 (C-5), 81.5 (C-7), 54.0 (C-8), 39.3 (C-6), 13.6 (CH_3) ppm. IR: $\tilde{\nu}$ = 1757 cm^{-1}.

Irradiation of Photosubstrate 24: According to the general procedure a solution of **24** (100 mg, 0.7 mmol) in a 9:1 mixture of acetonitrile/acetone (30 mL) was irradiated for 2 h at 300 nm. The solvent was removed and the residue (mixture of **27** and **28** in a ratio 66:34 according to ^{1}H NMR) was purified by chromatography (hexanes//EtOAc, 4:1) to give **27** as a light yellow oil (30 mg, 30%). Data for 7-butyl-2-methyl-8-methylene-4-oxatricyclo[3.3.0.0^{2,7}]octan-3-one (**27**): ^{1}H NMR: δ = 4.94 (dd, J = 4.0, 3.0 Hz, 1 H, 5-H), 4.63 (s, 1 H, =CH*H*), 4.62 (s, 1 H, =C*H*H), 3.23 (d, J = 2.5 Hz, 1 H, 1-H), 1.99 (dd, J = 12.0, 4.0 Hz, 1 H, 6-H), 1.70 (d, J = 12.0 Hz, 1 H, 6′-H), 1.65–1.53 (m, 2 H, CH_2 *n*Bu), 1.34–1.23 (m, 7 H, 2 × CH_2, CH_3) 0.86 (t, J = 7.2 Hz, 1 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 177.0 (C-3), 153.9 (C-8), 94.7 (=CH_2), 78.3 (C-5), 61.4 (C-1), 60.5 (C-2), 54.9 (C-7), 38.4 (C-6), 26.9 (CH_2), 25.8 (CH_2), 23.3 (CH_2), 14.1 (CH_3, *n*Bu), 8.9 ppm. IR: $\tilde{\nu}$ = 1763 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{13}H_{19}O_2$ 207.1385; found 207.1387 [M + H]$^+$.

Irradiation of Photosubstrate 31: According to the general procedure a solution of **31** (1.47 g, 5.96 mmol) in a 9:1 mixture of acetonitrile/acetone (150 mL) was irradiated for 1.5 h at 300 nm. The solvent was removed and the residue purified by chromatography (hexanes/EtOAc, 8:2) to give **32** as a colorless crystalline solid (1.03 g, 70%); m.p. 37–39 °C. ^{1}H NMR: δ = 4.70 (s, 1 H, =CH*H*), 4.62 (d, J = 4.0 Hz, 1 H, CH), 4.55 (s, 1 H, =C*H*H), 2.05 (dt, J = 13.5, 2.8 Hz, 1 H), 1.99 (dd, J = 11.6, 4.0 Hz, 1 H), 1.93–1.88 (m, 1 H), 1.72 (d, J = 12.0 Hz, 1 H), 1.64–1.43 (m, 6 H), 1.35–1.26 (m, 4 H), 1.18–1.15 (m, 1 H), 1.02 (dt, J = 13.5, 3.3 Hz, 1 H), 0.89 (t, J = 7.2 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 175.9 (C=O), 154.2 (>C=), 93.9 (CH_2), 80.1 (CH), 64.3 (C_q), 59.4 (C_q), 55.2 (C_q), 39.1 (CH_2), 26.9 (CH_2), 25.6 (CH_2), 22.8 (CH_2), 21.5 (CH_2), 20.2 (CH_2), 19.3 (CH_2), 19.2 (CH_2), 13.7 (CH_3) ppm. IR: $\tilde{\nu}$ = 2929, 1766, 1690 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{16}H_{23}O_2$ 247.1698; found 247.1699 [M + H]$^+$. $C_{16}H_{22}O_2$ (246.35): calcd. C 78.01, H 9.00; found C 78.13, H 9.43.

5-Butyl-4-methyl-3-methylene-3,3a,6,6a-tetrahydro-2*H*-cyclopenta-[*b*]furan-2-one (28): Cycloadduct **27** was heated in vacuo at 70 °C for 5 h to furnish **28** (23 mg, 75%) as a light yellow oil after chromatographic purification (hexanes/EtOAc, 9:1). ^{1}H NMR: δ = 6.21 (d, J = 2.0 Hz, 1 H, =CH*H*), 5.65 (d, J = 1.5 Hz, 1 H, =C*H*H), 5.02 (t, J = 6.3 Hz, 1 H, 7-H), 3.84–3.76 (m, 1 H, 8-H), 2.83–2.71 (m, 1 H, 6-H), 2.62 (d, J = 18.0 Hz, 1 H, 6′-H), 2.07 (t, J = 7.5 Hz, 2 H, CH_2 *n*Bu), 1.60 (s, 3 H, CH_3), 1.41–1.20 (m, 2 H, CH_2 *n*Bu), 1.28 (m, 2 H, CH_2 *n*Bu), 0.90 (t, J = 7.3 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 170.7 (C-2), 136.5 (>C=), 135.9 (>C=), 128.2 (>C=), 121.5 (= CH_2), 79.8 (C-7), 55.3 (C-8), 42.1 (C-6), 30.1 (CH_2), 28.2 (CH_2), 22.7 (CH_2), 14.2 (CH_3, *n*Bu), 10.9 (CH_3) ppm. IR: $\tilde{\nu}$ = 1759 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{13}H_{19}O_2$ 207.1385; found 207.1387 [M + H]$^+$.

Thermolysis of 3: After heating **3**[2b] (450 mg, 2.36 mmol) in 45 mL of DMF for 14 h at 140 °C, the solvent was removed in vacuo and the residue was purified by chromatography (hexanes/EtOAc, 9:1) to provide an inseparable mixture of **2** and **29** (ratio 47:53). The mixture was allowed to crystallize from hexanes resulting in the isolation of **29** as a crystalline compound (65 mg, 14%); m.p. 69–71 °C. ^{1}H NMR: δ = 6.99 (t, J = 3.6 Hz, 1 H, =CH), 5.46–5.40 (m, 1 H, =CH), 4.56 (d, J = 4.8 Hz, 1 H), 2.97–2.68 (m, 1 H), 2.66–2.54 (m, 1 H), 2.51–2.40 (m, 1 H), 2.39–2.44 (m, 1 H), 1.99–1.81 (m, 3 H), 1.80–1.71 (m, 3 H), 1.69–1.56 (m, 1 H) ppm. ^{13}C NMR: δ = 169.8 (C=O), 142.1 (=CH), 136.7 (>C=), 130.7 (>C=), 123.9 (=CH), 89.9 (CH), 56.1 (C_q), 36.2 (CH_2), 29.4 (CH_2), 24.2 (CH_2), 18.6 (CH_2), 14.7 (CH_3) ppm. IR: $\tilde{\nu}$ = 1745 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{12}H_{15}O_2$ 191.1072; found 191.1075 [M + H]$^+$.

X-ray Crystal Structure Analysis of 29: $C_{12}H_{14}O_2$, M = 190.24, T = 293 K, λ = 1.5418 Å, triclinic, $P\bar{1}$, a = 5.8759(4) Å, b = 7.857(1) Å, c = 11.694(10) Å, α = 74.40(3)°, β = 85.447(16)°, γ = 74.232(8)°, V = 500.4(4) Å^3, Z = 2, D_x = 1.26 g cm^{-3}, 1444 observed unique reflections, R_1 = 0.052.

CCDC-773803 contains the supplementary crystallographic data for **29**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Thermolysis of 32: After heating **32** (700 mg, 2.84 mmol) in 70 mL of DMF for 14 h provided at 140 °C, the solvent was removed and the residue purified by chromatography (5% EtOAc in hexanes) to provide a mixture of **31** and **33** (10:90). The chromatographic fractions containing both products were collected and concentrated in vacuo. The residue was recrystallized from hexanes resulting in the isolation of **33** as a crystalline solid (343 mg, 49%); m.p. 52–54 °C. ^{1}H NMR: δ = 6.95 (t, J = 2.0 Hz, 1 H=CH), 4.48 (d, J = 4.8 Hz, 1 H, CH), 2.79–2.69 (m, 1 H, CH), 2.57–2.49 (m, 1 H, CH), 2.49–2.38 (m, 1 H, CH), 2.37–2.21 (m, 1 H, CH), 2.14–2.06 (m, 2 H, CH_2 *n*Bu), 1.99–1.76 (m, 3 H, CH, CH_2), 1.66–1.55 (m, 4 H, CH_3, CH), 1.48–1.23 (m, 4 H, 2 × CH_2 *n*Bu), 0.91 (t, J = 7.2 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 170.2 (C=O), 136.1 (CH), 135.3 (C_q), 132.9 (C_q), 131.3 (C_q), 88.3 (CH), 57.3 (CH), 39.2 (CH_2), 29.8

(CH_2), 29.6 (CH_2), 27.9 (CH_2), 24.2 (CH_2), 22.2 (CH_2), 18.6 (CH_2), 13.8 CH_3, (*n*Bu), 11.9 (CH_3) ppm. IR: $\tilde{\nu}$ = 1753 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{16}H_{23}O_2$ 247.1698; found 247.1696 $[M + H]^+$. $C_{16}H_{22}O_2$: calcd. C 78.01, H 9.00; found C 77.31, H 9.27.

(3*S,7a*R**)-1-Butyl-7a-(hydroxymethyl)-8-methyleneoctahydro-1,3a-methanoinden-3-ol (34):** To a cooled solution of $LiAlH_4$ (15.0 mmol) in THF (45 mL) was added dropwise a solution of lactone **32** (1.170 g, 4.75 mmol) in THF (30 mL). The resulting mixture was stirred for 1 h. The reaction was quenched by careful addition of ethyl acetate (10 mL), followed by saturated Na_2SO_4 solution (5 mL). The mixture was stirring for 30 min, treated with solid Na_2SO_4, filtered through Celite, and concentrated in vacuo. Purification by recrystallization from hexanes/EtOAc afforded diol **21** (0.862 g, 3.34 mmol, 73%) as a colorless solid; m.p. 123–124 °C. ^{1}H NMR: δ = 4.47 (s, 1 H, =C*H*H), 4.34 (s, 1 H, =CH*H*), 4.04–3.98 (m, 2 H, C*H*OH, *H*CHOH), 3.79 (d, *J* = 11.5 Hz, 1 H, HC*H*OH) 2.65 (br. s, 1 H, OH), 2.53 (br. s, 1 H, OH), 1.99–1.91 (m, 2 H), 1.81–1.40 (m, 11 H), 1.34–1.22 (m, 3 H), 1.14–1.11 (m, 1 H), 0.89 (t, *J* = 7.2 Hz, 3 H) ppm. ^{13}C NMR: δ = 159.2 (>C=), 92.1 (=CH_2), 73.2 (CHOH), 66.0 (CH_2OH), 61.3 (C_q), 60.0 (C_q), 46.2 (C_q), 39.9 (CH_2), 31.7 (CH_2), 27.8 (CH_2), 26.7 (CH_2), 23.5 (CH_2), 22.0 (CH_2), 21.6 (CH_2), 21.1 (CH_2), 14.0 (CH_3) ppm. IR: $\tilde{\nu}$ = 3300, 2927, 2860 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{16}H_{27}O_2$ 251.2011; found 251.2011 $[M + H]^+$. $C_{16}H_{26}O_2$ (250.38): calcd. C 76.75, H 10.47; found C 76.74, H 10.48.

Silyl Ether 35: To a stirred solution of diol **34** (0.830 g, 3.32 mmol) in DMF (20 mL) was added *tert*-butyldimethylsilyl chloride (0.745 g, 4.49 mmol) and imidazole (1.59 g, 23.35 mmol). The resulting mixture was stirred overnight at room temperature and then diluted with ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (2× 25 mL). The organic layers were combined and washed with water (3× 80 mL), dried with $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (hexanes/EtOAc, 20:1) gave **35** as a colorless oil (0.713 g, 1.96 mmol, 59%). ^{1}H NMR: δ = 4.45 (s, 1 H, =C*H*H), 4.31 (s, 1 H, =CH*H*), 3.91–3.83 (m, 3 H), 3.51 (d, *J* = 7.2 Hz, 1 H, HC*H*OH), 1.92 (dd, *J* = 12.0, 7.6 Hz, 1 H), 1.87 (dd, *J* = 12.0 2.4 Hz, 1 H), 1.69–1.59 (m, 5 H), 1.53–1.35 (m, 5 H), 1.31–1.12 (m, 4 H), 0.90–0.86 (m, 12 H), 0.86 (s, 3 H, $SiCH_3$), 0.76 (s, 3 H, $SiCH_3$) ppm. ^{13}C NMR: δ = 159.6 (>C=), 91.9 (=CH_2), 73.3 (CHOH), 65.0 (CH_2OH), 61.6 (C_q), 60.2 (C_q), 46.1 (C_q), 40.4 (CH_2), 30.3 (CH_2), 27.7 (CH_2), 26.9 (CH_2), 25.8 [CH_3 SiC(*C*H_3)$_3$], 23.5 (CH_2), 21.9 (CH_2), 21.7 (CH_2), 20.9 (CH_2), 18.1 [Si*C*(CH_3)$_3$], 14.0 (CH_3 *n*Bu), –5.48 ($SiCH_3$), –5.73 ($SiCH_3$) ppm. IR: $\tilde{\nu}$ = 3323, 2928, 2857, 1065, 834 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{22}H_{41}O_2Si$ 365.2876; found 365.2870 $[M + H]^+$.

Benzyl Ether 37: To a stirred solution of silyl ether **35** (0.690 g, 1.892 mmol) in THF (12 mL) was added benzyl bromide (0.450 mL, 0.648 g, 3.79 mmol) and sodium hydride (0.167 g, 4.16 mmol, 60 wt.-% dispersion in mineral oil). The resulting mixture was stirred at room temperature for 30 min. Tetra-*n*-butylammonium iodide was added (catalytic) and stirring was continued overnight. The reaction was quenched with ice water. The mixture was extracted with diethyl ether (3× 15 mL). The combined organic layers were then washed with water (2× 40 mL). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (hexanes/EtOAc, 50:1) yielded **37** as a clear oil (0.847 g, 1.86 mmol, 99%). ^{1}H NMR: δ = 7.34–7.25 (m, 5 H, Ph), 4.56 (d, *J* = 8 Hz, 1 H, Ph*H*CHO), 4.49 (s, 1 H, =C*H*H), 4.43 (d, *J* = 12.5 Hz, 1 H, PhHC*H*O), 4.32 (s, 1 H, =CH*H*), 4.24 (d, *J* = 11 Hz, 1 H, *H*CHOSi), 3.65 (t, *J* = 5 Hz, 1 H, *CH*OBn), 3.52 (d, *J* = 11 Hz, 1 H, HC*H*OSi), 2.04 (d, *J* = 12 Hz, 1 H), 1.90 (m, 2 H), 1.62–1.14 (m, 13 H), 0.88 (m, 12 H), 0.02 [s, 6 H, Si(CH_3)$_2$] ppm. ^{13}C NMR: δ = 159.5 (>C=), 139.1 (C_q Ph), 129.0 (CH Ph), 128.4 (CH Ph), 127.2 (CH Ph), 92.2 (=CH_2), 80.3 (*CH*OBn), 70.9 (Ph*CH*$_2$O), 60.4 (C_q), 59.9 (C_q), 59.6 (CH_2OSi), 47.1 (C_q), 40.4 (CH_2), 37.0 (CH_2), 27.6 (CH_2), 25.8 [SiC(*CH*$_3$)$_3$], 25.0 (CH_2), 23.7 (CH_2), 22.1 (CH_2), 21.3 (CH_2), 20.9 (CH_2), 18.2 (CH_2), 14.0 (CH_3 *n*Bu), –5.4 ($SiCH_3$), –5.6 (CH_3) ppm. IR: $\tilde{\nu}$ = 2928, 1227, 1027, 834 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{29}H_{47}O_2Si$ 455.3345; found 455.3340 $[M + H]^+$.

[(3*S,7a*R**)-3-(Benzyloxy)-1-butyl-8-methyleneoctahydro-1,3a-methanoinden-7a-yl]methanol (38):** To a stirred solution of **37** (0.847 g, 1.86 mmol) in CH_2Cl_2/MeOH (12.5 mL, 9:1) was added camphorsulfonic acid (0.173 g, 0.744 mmol). The resulting mixture was stirred overnight. The reaction was quenched with saturated $NaHCO_3$ solution. The layers were separated and the aqueous layer was extracted with ethyl acetate (2× 20 mL). The organic layers were combined and washed with water (2× 40 mL). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (hexanes/EtOAc, 20:1) yielded **38** as a light yellow oil (0.446 g, 1.31 mmol, 70%). ^{1}H NMR: δ = 7.37–7.26 (m, 5 H, Ph), 4.65 [d, *J* = 12.0 Hz, 1 H (Ph*H*CHO)], 4.50–4.47 (m, 2 H, =C*H*H, PhHC*H*O), 4.35 (s, 1 H, =CH*H*), 3.98 [d, *J* = 12.0 Hz, 1 H, (*H*CHOH)], 3.78 (dd, *J* = 7.2, 2.0 Hz, 1 H, C*H*OBn), 3.71 (d, *J* = 12.0 Hz, 1 H, HC*H*OH), 2.76 (br. s, 1 H, OH), 2.05 (dd, *J* = 12.0, 2.4 Hz, 1 H), 1.88–1.12 (m, 15 H), 0.91 (t, *J* = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 158.6 (>C=), 137.9 (C_q Ph), 128.3 (CH Ph), 127.5 (CH Ph), 127.4 (CH Ph), 92.1 (=CH_2), 80.2 (*CH*OBn), 71.3 (Ph*C*H_2O), 65.9 (CH_2OSi), 60.6 (C_q), 59.8 (C_q), 46.3 (C_q), 37.0 (CH_2), 31.3 (CH_2), 27.7 (CH_2), 26.6 (CH_2), 23.3 (CH_2), 21.8 (CH_2), 21.5 (CH_2), 21.4 (CH_2), 13.9 (CH_3) ppm. IR: $\tilde{\nu}$ = 3460, 2926, 1454, 1065, 733 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{23}H_{33}O_2$ 341.2481; found 341.2482 $[M + H]^+$.

(3*S,7a*S**)-3-(Benzyloxy)-1-butyl-7a-methyl-8-methyleneoctahydro-1,3a-methanoindene (39):** To a stirred solution of **38** (0.430 g, 1.263 mmol) in pyridine (6.4 mL) was added *p*-toluenesulfonyl chloride (0.489 g, 2.57 mmol). The resulting mixture was stirred overnight at room temperature. The reaction was quenched with water (2 mL) and stirring was continued for 1 h. The mixture was further diluted with CH_2Cl_2 (25 mL). The layers were separated and the organic layer was washed with 10% $KHSO_4$ solution (3× 20 mL). The organic layer was dried with $MgSO_4$ and then concentrated in vacuo to afford the tosylate (0.578 g) as an oil which was used for the next step without further purification. ^{1}H NMR: δ = 7.72 (d, *J* = 8.0 Hz, 2 H, 2× CH Ts), 7.36–7.21 (m, 7 H, 2× CH Ts, Ph), 4.75 (d, *J* = 10.5 Hz, 1 H, Ph*H*CHO), 4.56 (s, 1 H, =C*H*H), 4.44 (d, *J* = 12.0 Hz, 1 H, PhHC*H*O), 4.36 (s, 1 H, =CH*H*), 4.33 (d, *J* = 14.5 Hz, 1 H, *H*CHOTs), 3.99 (d, *J* = 11.0 Hz, 1 H, HC*H*OTs), 3.60 (dd, *J* = 7.0, 2.5 Hz, 1 H, C*H*OBn), 2.42 (s, 3 H, SO_3CH_3), 1.92–1.83 (m, 2 H), 1.56–1.02 (m, 16 H), 0.92 (t, *J* = 7.5 Hz, 3 H, CH_3) ppm. To a solution of crude tosylate in THF (22 mL) was added lithium triethylborohydride (1 M *in* THF, 5.05 mL, 5 equiv.). The reaction mixture was refluxed for 18 h and then cooled to 0 °C. The reaction was quenched with ice water (6 mL) and the layers were separated. The aqueous layer was extracted with diethyl ether (3× 25 mL), the combined organic layers were then washed with water (2× 75 mL). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (hexanes/EtOAc, 20:1) afforded **39** as a colorless oil (0.143 g, 0.436 mmol, 43% over two steps). ^{1}H NMR: δ = 7.34–7.24 (m, 5 H, Ph), 4.58 (d, *J* = 12.4 Hz, 1 H, Ph*H*CHO), 4.47–4.44 (m, 2 H, PhHC*H*O, =C*H*H), 4.30 (s, 1 H, =CH*H*), 3.65 (dd, *J* = 7.2, 2.8 Hz, 1 H, C*H*OBn), 1.93–1.83 (m, 2 H), 1.73–1.22 (m, 14 H), 1.15 (s, 3 H, CH_3), 0.90 (t, *J* = 6.8 Hz, 3 H, CH_3 *n*Bu)

ppm. ^{13}C NMR: δ = 160.4 (>C=), 139.3 (C_q Ph), 128.2 (CH Ph), 127.1 (CH Ph), 127.0 (CH Ph), 91.9 (=CH_2), 81.4 (*CH*OBn), 71.0 (Ph*C*H_2O), 60.5 (C_q), 59.3 (C_q), 42.4 (C_q), 37.3 (CH_2), 32.7 (CH_2), 27.7 (CH_2), 26.5 (CH_2), 23.7 (CH_2), 22.4 (CH_2), 22.8 (CH_2), 20.6 (CH_2), 14.1 (CH_3), 12.5 (CH_3 *n*Bu) ppm. IR: $\tilde{\nu}$ = 2927, 1686, 1454, 1104, 730 cm^{-1}. HR-MS: *m*/*z* calcd. for $C_{23}H_{33}O$ 325.2531; found 325.2528 [M + H]$^+$.

(4*S,5*R**)-4-(Benzyloxy)-2-butyl-1,6-dimethylspiro[4.5]deca-1,6-diene (40):** A sample of **39** (20 mg, 0.062 mmol) was dissolved in [D_6]DMSO. The solution was heated at 180 °C for 4 h, after which ^{1}H NMR showed complete conversion of starting material. The mixture was then cooled and diluted with diethyl ether (10 mL) and washed with water (2 × 10 mL). The aqueous layers were extracted with diethyl ether (2 × 20 mL). The organic layer was dried with MgSO4 and concentrated in vacuo to give **40** (9 mg, 45%) ^{1}H NMR: δ = 7.34–7.26 (m, 5 H, Ph), 5.67 (br. s, 1 H, =CH), 4.60 (d, *J* = 12.4 Hz, 1 H, Ph*H*CHO), 4.56 (d, *J* = 12.4 Hz, 1 H, PhHC*H*O), 3.80 (dd, *J* = 7.9, 5.3 Hz, 1 H, *CH*OBn), 2.60 (dd, *J* = 16.0, 7.9 Hz, 1 H), 2.35–2.29 (m, 1 H), 2.17–2.11 (m, 1 H), 2.09–1.99 (m, 3 H), 1.71–1.59 (m, 7 H), 1.46 (br. s, 3 H, CH_3), 1.41–1.25 (m, 6 H), 0.92 (t, *J* = 7.2 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 139.4 (C_q Ph), 135.6 (>C=), 134.9 (>C=), 133.8 (>C=), 128.2 (CH Ph), 128.1 (CH Ph), 127.4 (CH Ph), 127.1 (CH Ph), 125.2 (CH=), 86.9 (*CH*OBn), 71.4 (Ph*C*H_2O), 58.3 (C_q), 41.4 (CH_2), 34.7 (CH_2), 30.0 (CH_2), 28.4 (CH_2), 25.8 (CH_2), 22.5 (CH_2), 21.6 (CH_3), 19.4 (CH_2), 14.0 (CH_3), 10.8 (CH_3 *n*Bu) ppm. IR: $\tilde{\nu}$ = 2926, 1454, 1095 cm^{-1}.

(3*S,7a*S**)-3-(Benzyloxy)-1-butyl-8-(hydroxymethyl)-7a-methyloctahydro-1,3a-methanoinden-8-ol (41):** To a stirred mixture of *tert*-butyl alcohol (1.3 mL) and pyridine (90 μL) at 45 °C was added alkene **39** (43.5 mg, 0.134 mmol). To this mixture was added OsO_4 (4 wt.-% in water, 1.23 mL, 0.201 mmol) and stirring was continued for 20 h. The reaction was quenched with 20% sodium bisulfite solution (2 mL) and stirred for 45 min at room temperature. The mixture was further diluted with water (3 mL) and extracted with EtOAc (4 × 10 mL). The combined organic layers were washed with water (4 × 20 mL). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Column chromatography (EtOAc/hexanes, 1:8) yielded **41** as a colorless oil (21.0 mg, 44%) ^{1}H NMR: δ = 7.35–7.24 (m, 5 H, Ph), 4.61 (d, *J* = 12.0 Hz, 1 H, Ph*H*CHO), 4.48 (d, *J* = 10.0 Hz, 1 H, *H*CHOH), 4.45 (d, *J* = 8.8 Hz, 1 H), 4.15–4.09 (m, 2 H), 2.21 (dd, *J* = 11.2, 7.2 Hz, 1 H), 2.05–1.98 (m, 1 H), 1.82 (dd, *J* = 11.2, 2.4 Hz, 1 H), 1.66–1.55 (m, 4 H), 1.45–1.32 (m, 5 H), 1.30–1.21 (m, 6 H), 1.18 (s, 3 H, CH_3), 0.88 (t, *J* = 7.2 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 139.6 (C_q Ph), 128.2 (CH Ph), 127.1 (CH Ph), 127.0 (CH Ph), 82.0 (*C*HOBn), 81.4 (C_q), 71.6 (Ph*C*H_2O), 66.6 (CH_2OH), 57.9 (C_q), 57.2 (C_q), 40.6 (C_q), 36.1 (CH_2), 31.6 (CH_2), 28.0 (CH_2), 26.3 (CH_2), 23.7 (CH_2), 22.2 (CH_2), 21.1 (CH_2), 20.9 (CH_3), 20.2 (CH_2), 14.0 (CH_3 *n*Bu) ppm. IR: $\tilde{\nu}$ = 3450, 2915, 1750, 1480 cm^{-1}.

(3*S,7a*S**)-3-(Benzyloxy)-1-butyl-7a-methyloctahydro-1,3a-methanoinden-8-one (42):** To a solution of diol **41** (18.0 mg, 0.051 mmol) in acetone/water (1:1 v/v%, 2.25 mL) was added sodium periodate (23.3 mg, 0.109 mmol). The resulting mixture was stirred for 2 d at room temperature. Acetone was then removed in vacuo. The resulting suspension was dissolved in EtOAc (10 mL) and washed with brine (2 × 15 mL). The organic layer was dried with $MgSO_4$ and concentrated in vacuo. Column chromatography (EtOAc/hexanes, 1:15) yielded **42** as a colorless oil (14.8 mg, 90%). ^{1}H NMR: δ = 7.33–7.25 (m, 5 H, Ph), 4.58 (d, *J* = 12.4 Hz, 1 H, Ph*H*CHO), 4.46 (d, *J* = 12.0 Hz, 1 H, PhHC*H*O), 3.77 (dd, *J* = 7.2, 3.6 Hz, 1 H, C*H*OBn), 2.10–2.00 (m, 2 H) 1.78 (dd, *J* = 13.2, 3.6 Hz, 1 H), 1.63–1.15 (m, 16 H), 0.89 (t, *J* = 7.2 Hz, 3 H, CH_3 *n*Bu) ppm. ^{13}C NMR: δ = 205.3 (C=O), 138.5 (C_q Ph), 128.3 (CH Ph), 127.5 (CH Ph), 127.2 (CH Ph), 74.8 (*CH*OBn), 70.9 (Ph*C*H_2O), 69.8 (C_q), 69.1 (C_q), 37.1 (C_q), 34.6 (CH_2), 34.4 (CH_2), 27.3 (CH_2), 23.9 (CH_2), 23.4 (CH_2), 22.6 (CH_2), 21.3 (CH_2), 19.7 (CH_2), 14.3 (CH_3), 13.9 (CH_3 *n*Bu) ppm. IR: $\tilde{\nu}$ = 2930, 1792, 1455, 1101, 733 cm^{-1}. HR-MS (FAB) calcd. for $C_{22}H_{31}O_2$ 327.2324; found 327.2323 [M + H]$^+$.

Acknowledgments

We wish to thank Jan A. J. Geenevasen for his generous help to analyse many NMR spectra and Lianne M. Jongens and Soraya N. Sluijter for their synthetic contributions.

[1] For recent reviews, see, for example: a) T. Bach, J. P. Hehn, *Angew. Chem. Int. Ed.* **2011**, *50*, 1000–1045; b) N. Hoffmann, *Chem. Rev.* **2008**, *108*, 1052–1103; c) J. Iriondo-Alberdi, M. F. Greaney, *Eur. J. Org. Chem.* **2007**, 4801–4815.

[2] a) B. T. B. Hue, J. Dijkink, S. Kuiper, K. K. Larson, F. S. Guziec Jr., K. Goubitz, J. Fraanje, H. Schenk, J. H. van Maarseveen, H. Hiemstra, *Org. Biomol. Chem.* **2003**, *1*, 4364–4366; b) B. T. B. Hue, J. Dijkink, S. Kuiper, S. van Schaik, J. H. van Maarseveen, H. Hiemstra, *Eur. J. Org. Chem.* **2006**, 127–137; c) for a recent review on [2+2] cycloadditions of allenes, see: B. Alcaide, P. Almendros, C. Aragoncillo, *Chem. Soc. Rev.* **2010**, *39*, 783–816.

[3] a) C. W. Jefford, A. W. Sledeski, J. Boukouvalas, *Helv. Chim. Acta* **1989**, *72*, 1362–1370; b) C. W. Jefford, A. W. Sledeski, J.-C. Rossier, J. Boukouvalas, *Tetrahedron Lett.* **1990**, *31*, 5741–5744.

[4] J. Pornet, B. Randrianoelina, L. Miginiac, *J. Organomet. Chem.* **1979**, *174*, 1–13.

[5] G. Lutteke, R. AlHussainy, P. J. Wrigstedt, B. T. B. Hue, R. de Gelder, J. H. van Maarseveen, H. Hiemstra, *Eur. J. Org. Chem.* **2008**, 925–933.

[6] G. Casiraghi, G. Rassu, P. Spanu, L. Pinna, *J. Org. Chem.* **1992**, *57*, 3760–3763.

[7] M. N. Wrobel, P. Margaretha, *Helv. Chim. Acta* **2003**, *86*, 515–521.

[8] a) J. Meinwald, J. K. Crandall, *J. Am. Chem. Soc.* **1966**, *88*, 1292–1301; b) G. Mehta, S. R. Singh, V. Gagliardini, U. D. Priyakumar, G. N. Sastry, *Tetrahedron Lett.* **2001**, *42*, 8527–8530.

[9] a) P. Conti, A. P. Kozikowski, *Tetrahedron Lett.* **2000**, *41*, 4053–4056; b) N. Jullian, I. Brabet, J.-P. Pin, F. C. Acher, *J. Med. Chem.* **1999**, *42*, 1546–1555.

[10] M. Abe, E. Torii, M. Nojima, *J. Org. Chem.* **2000**, *65*, 3426–3431.

[11] J.-L. Ripoll, Y. Vallée, *Synthesis* **1993**, 659–677.

[12] J. M. Cassady, S. R. Byrn, I. K. Stamos, S. M. Evans, A. McKenzie, *J. Med. Chem.* **1978**, *21*, 815–819.

[13] a) H. M. R. Hoffmann, J. Rabe, *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 94–110; b) R. R. A. Kitson, A. Millemaggi, R. J. K. Taylor, *Angew. Chem. Int. Ed.* **2009**, *48*, 9426–9451.

[14] H. Schenk, R. A. J. Driessen, R. de Gelder, K. Goubitz, H. Nieboer, I. E. M. Brüggemann-Rotgans, P. Diepenhorst, *Croat. Chem. Acta* **1999**, *72*, 593–606.

[15] W. K. Appel, T. J. Greenhough, J. R. Scheffer, J. Trotter, *J. Am. Chem. Soc.* **1979**, *101*, 213–215.

[16] See, e. g.: D. Bellus, B. Ernst, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 797–827.

Received: February 23, 2011
Published Online: May 2, 2011

