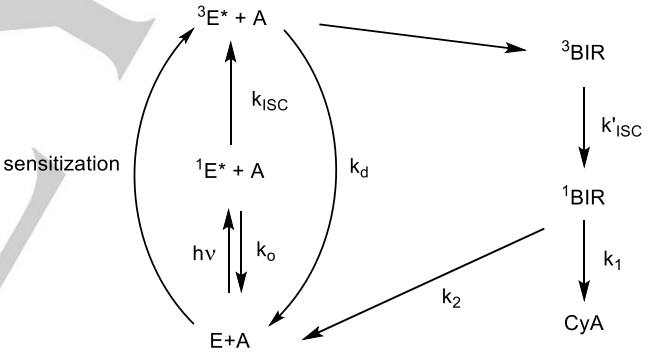
A Study on the Photoreaction of 2(5*H*)-Furanones with Substituted Acetylenes: Evidences for a Mechanistic Reformulation

Ramon Flores,[a] Josep Font,[a] Ramon Alibés,*[a] and Marta Figueredo*[a]

Abstract: The photoreaction of 2(5*H*)-furanones with alkynes has been investigated. The complexity of this process is evidenced by the variety of isolated products, which have allowed disclosing interesting mechanistic aspects. When the reaction is performed in acetonitrile under direct excitation, in addition to the primary [2+2] cycloadducts, products derived from an 1,3-acyl shift rearrangement are also formed. For unsymmetrical alkynes, the rearrangement of the head-to-tail primary adducts produces new regioisomers and, when the starting furanone is chiral, this rearrangement inverts the relative *anti/syn* geometry of the primary cycloadducts. In the reactions performed in acetone under photosensitized conditions, rearranged products were never detected, supporting that the 1,3-acyl shift takes place from the singlet excited state S_1 of the β,γ-unsaturated lactone. When bis(trimethylsilyl)acetylene is used as the alkyne partner, the major photoproducts are monocyclic bis(trimethylsilyl)lactones.

Introduction

The cyclobutane motif is present in many natural products and other biologically significant compounds,[1] including terpenes,[2] alkaloids[3] and nucleoside analogs,[4] among others. Some of these compounds are polyfunctionalized molecules, wherein the cyclobutane moiety bears several subtituents attached to the ring through carbon-carbon and/or carbon-heteroatom bonds and, occasionally, the four membered carbocycle is embodied in a more intricate polycyclic structure. Moreover, the cyclobutane ring strain may be used as the driving force to propitiate useful skeletal transformations, such as atom insertion, with concomitant ring expansion, or scission to deliver a four-carbon-atom fragment.[5] Cyclobutene compounds have also proved to be useful for synthetic applications.[6] Additions to the double bond provide a route for further substitution, whilst thermal electrocyclic ring opening delivers dienes.[7] Consequently, developing efficient accesses to cyclobutane and cyclobutene formation has been and still is the object of many synthetic organic chemists. One of the most usual methodologies to synthesize cyclobutanes is the photochemically induced [2+2] cycloaddition of simple alkenes to carbon-carbon double bonds activated by conjugation with an electron-withdrawing group.[8] It is broadly accepted that this kind of process involves the excited triplet state of the conjugated system, for instance an enone (E), and the ground state of the simple alkene partner (A) (Scheme 1).[9] Accordingly, nπ* or ππ* excitation of the photoactive alkene leads to the lowest excited singlet state (^{1}E), which evolves to the excited triplet state (^{3}E) by an intersystem crossing process. Alternatively, the triplet state ^{3}E may be reached by energy transfer from an excited sensitizer with a higher energy triplet state. Once the triplet 1,4-biradical intermediate (BIR) is formed, spin inversion gives a singlet biradical, which can either revert to ground state starting materials or combine intramolecularly to afford the cycloadducts (CyA).



Scheme 1. General mechamism for the photochemically induced [2+2] cycloaddition of a conjugate alkene (E) to a simple alkene (A).

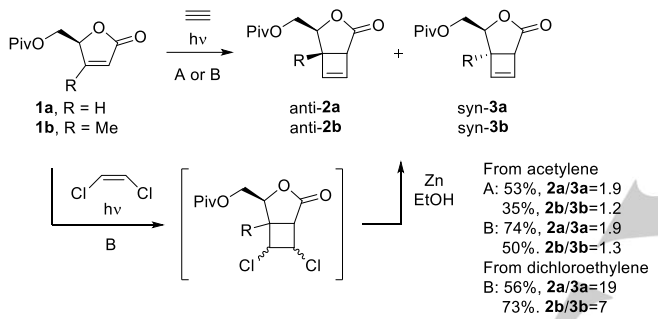
Along years, our group has investigated in deep the photoreactions of chiral 2(5*H*)-furanones to alkenes. During these studies, we were able to find conditions to achieve yields and facial selectivities good enough for applying some of these cycloadditions as key steps in the synthesis of diverse compounds with verified or potential biological activity.[10] In contrast, the photoreactions of the same furanones with acetylene were considerably less effective both in terms of yield and diastereoselectivity (Scheme 2), providing complex crude products, wherein we identified several byproducts derived from photoreduction and/or electrocyclic ring opening of the primary cycloadducts.[11] These observations were consistent with previous results described for the photoactivated cycloaddition of alkynes to enones.[12] In our laboratories, these difficulties were partially solved by applying a two-step protocol, where 1,2-dichloroethylene was used as an acetylene surrogate in the

[a] Dr. R. Flores, Prof. Dr. J. Font, Dr. R. Alibés, Prof. Dr. M. Figueredo
Departament de Química
Universitat Autònoma de Barcelona
08193 Bellaterra (Spain)
E-mail: ramon.alibes@uab.cat; marta.figueredo@uab.es

Supporting information for this article is given via a link at the end of the document.

photo-process and then the chlorine was reductively eliminated.[13]

In a recently published study on the photochemical [2+2] cycloaddition of several chiral 2(5*H*)-furanones to trialkylsilylacetylene, D'Annibale and co-workers isolated *syn* cyclobutenes as the major products and, after performing some theoretical calculations, they concluded that the regio- and stereoselectivity of the process depend on the relative stability of the intermediate diradicals.[14] The preferred synfacial selectivity observed by these authors was in contrast with our previous findings, since the photoreactions between furanones **1a-b** and acetylene showed the opposite antifacial preference. Intrigued by this discordance and with the aim of acquiring additional insights regarding the synthetic potential and mechanistic aspects of the photoreactions between 2(5*H*)-furanones and alkynes, we have extended our studies to symmetrical and non symmetrical trimethylsilyl- and hydroxymethylacetylenes. The results of these investigations are reported herein.



Scheme 2. Alternative pathways for the preparation of cyclobutenes from 2(5*H*)-furanones **1** through [2+2] photocycloadditions under sensitized (A: acetone/pyrex) or direct (B: acetonitrile/quartz) irradiation.

Results and Discussion

The lactones selected for our study were the simple crotonolactone, **4**, where the regioselectivity will not be influenced by any substituent of the ring, and the chiral (–)-(*S*)-5-acetyloxymethyl-2(5*H*)-furanone, **5** (Figure 1).

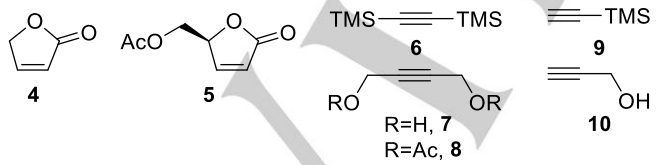
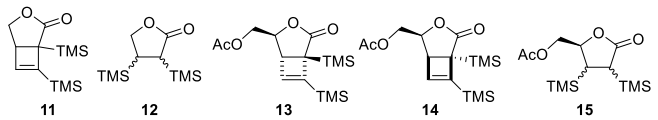


Figure 1. Selected furanones **4**-**5** and acetylenes **6**-**9** for the photochemical study.

The first assays were performed with the simplest furanone **4** and bis(trimethylsilyl)acetylene, **6**, because the use of symmetrical reactants reduces the number of predictable products. In a precedent study, Birkofer and Eichstädt described that irradiation through a quartz filter of a solution of maleic anhydride and bis(trimethylsilyl)acetylene in acetone containing benzophenone as a photosensitizer afforded the expected cyclobutene in 61% yield.[15] In our study, the photoreaction between **4** and **6** under identical conditions (Table 1, entry 1), after 4 h of irradiation, furnished only decomposition products. In view of that, we moved to the experimental conditions usually applied in our laboratories for similar reactions.[13] The irradiation of **4** and a five molar excess of acetylene **6** in acetonitrile through a quartz filter (entry 2) afforded two unexpected products, the rearranged bicyclic compound **11** (16% yield) and the bis(trimethylsilyl)lactone **12** (47% yield). Despite GC analysis showed some remaining furanone **4**, the irradiation was stopped after 4 hours because the incipient formation of multiple byproducts was detected. Similar ratios of compounds **11** and **12**, albeit in lower yields, were produced when the same reaction was run in hexane (entry 3) or diethyl ether (entry 4). In the last case, no starting furanone was recovered and the crude reaction mixture contained multiple unidentified decomposition products. Likewise, during the attempted irradiation in acetone through a pyrex filter (entry 5) the starting furanone **4** underwent decomposition to unidentified products. It is noteworthy that a primary cycloadduct was never detected in any of the investigated photoreactions and that the monocyclic bis(trimethylsilyl)lactone **12** was the major isolated product irrespective of the experimental conditions used.

Then, the reaction of the chiral lactone **5** with the same alkyne was attempted both under direct excitation in acetonitrile and photosensitized activation in acetone. The irradiation in acetonitrile (entry 6) was stopped after 4 hours, when some starting lactone was still present, and furnished a mixture of four products in 47% overall yield. Column chromatography of the mixture delivered two fractions; one of them contained two diastereomeric cyclobutenes, **13** and **14**, and the other one consisted of two diastereomers of the bis(trimethylsilyl)lactone **15**. Repeated chromatography allowed the isolation of a sample of the pure major product and enriched samples of the rest. NMR analyses of these samples lead to establish the relative configuration of **13** and **14**, but the stereochemistry of the isomers of **15** could not be unambiguously ascertained. The photoreaction in acetone (entry 7) consumed the starting furanone, but produced a complex mixture, from which we were unable to detect any identifiable compound.

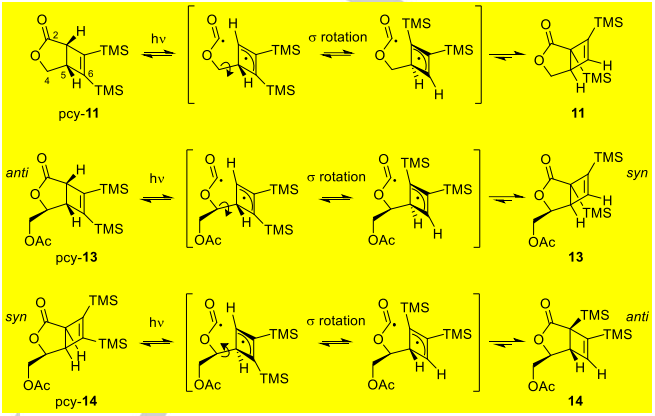
Table 1. Photoreaction of furanones **4** and **5** with alkyne **6**.[a]



Entry	Furanone	Solvent	Filter	Time [h]	Product (yield [%])[b]
1	**4**	acetone	quartz	5	—
2[c]	**4**	CH_3CN	quartz	6	**11**(16),**12**(47)
3[c]	**4**	hexane	quartz	6,5	**11**(6),**12**(25)
4	**4**	Et_2O	quartz	3,75	**11**(6),**12**(19)
5	**4**	acetone	pyrex	2	—
6[d]	**5**	CH_3CN	quartz	4	**13**+**14**(12),**15**(35)
7	**5**	acetone	pyrex	2	—

[a] Irradiations were performed in a nitrogen saturated solution; the external cooling bath was at –40°C and the jacket cooling liquid at –15°C. The substrate conversion was monitored by GC. [b] Yield of isolated products. [c] 25% of the starting furanone **4** was recovered. [d] 31% of the starting furanone **5** was recovered.

Several examples of photoreduction of a double bond by hydrogen radicals coming from solvent molecules have been described in the literature.[12a] We speculate that the formation of lactones **12** and **15** may result from a similar process with the participation of trimethylsilyl radical groups generated by photolysis of the carbon-silicon bond of the alkyne, a process that apparently prevails over the competitive [2+2] cycloaddition. On the other hand, the isolated cyclobutenes **11** and **13**-**14** must evolve from the undetected primary cycloadducts, pcy-**11**, pcy-**13** and pcy-**14**, respectively, through a 1,3-acyl shift rearrangement (Scheme 3). This kind of transformation was early observed during the photoreaction between 2-cyclopentenone and 2-butyne, where it was described that a photostationary state was reached when the primary cycloadduct and the rearranged derivative were irradiated separately.[16] Generally, the 1,3-acyl shift occurs from the β,γ-unsaturated carbonyl system excited singlet state S_1 and, hence, it is associated to photoreactions performed by direct irradiation through a quartz filter.[17] A plausible mechanism for this rearrangement implies an initial Norrish I type cleavage leading to an acyl-allyl biradical intermediate, followed by rotation around the C4-C5 bond and recombination of the biradical through the C2-C6 positions. In the cases under study, the equilibriums are totally displaced to the rearranged products **11**, **13** and **14**, most probably due to the high strain caused by the vicinal bulky TMS groups bonded to the sp^2 carbon atoms in the primary cycloadducts. It must be noted that the primary cycloadduct pcy-**13**, coming from the antifacial approach of the acetylene **6** to the chiral furanone **5**, is converted into the rearranged product **13**, wherein the cyclobutene moiety is oriented *syn* in relation to the oxymethyl substituent of the furanone. Similarly, the *syn* primary cycloadduct pcy-**14** evolves to the rearranged *anti* isomer **14**.

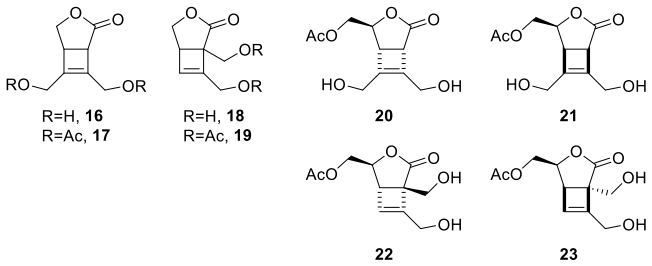


Scheme 3. Mechanistic pathway from the primary photocycloadducts to the isolated products **11**, **13** and **14**.

Next, the photoreactions of lactones **4** and **5** with alkynes **7** and **8** were investigated (Table 2). In contrast with the above results, the irradiation of an acetonitrile solution of the simplest furanone **4** with an excess of diol **7** furnished the primary [2+2] cycloadduct **16** as the major product, although the rearranged cyclobutene **18** was also isolated (entry 1). Because of the low solubility of **16** and **18** in most solvents evaluated, their purification was rather difficult and it was decided to assay the reaction of **4** with the bisacetyl derivative **8** (entry 3), which delivered the analogous photoproducts **17** and **19**, although in lower overall yield and a relatively higher proportion of the rearranged cyclobutene. The two reactions were also assayed by sensitized irradiation, but the starting materials evolved to complex mixtures of unidentified products (entries 2 and 4). Then, the chiral lactone **5** was irradiated in combination with the same alkynes. The photoreaction of **5** with diol **7** (entry 5), after 3 hours, delivered a mixture of two primary cycloadducts, **20** and **21**, and two rearranged cyclobutenes, **22** and **23**, in 49% overall yield, while 20% of the starting furanone **5** was recovered. Surprisingly, the irradiation of the same lactone in combination with the bisacetate **8** under identical conditions (entry 6) did not give any identifiable product, despite the starting furanone was totally consumed.

According to the above considerations concerning the stereochemical implications of the 1,3-acyl shift rearrangement, the transposed cyclobutanes **22** and **23** must respectively come from the *syn*, **21**, and *anti*, **20**, primary adducts. Therefore, the *anti:syn* estimated ratio assigned to the primary cycloadducts is 78:22 ([**20**+**23**]:[**21**+**22**]), which is consistent with a major approach of the alkyne through the less hindered face of the lactone.

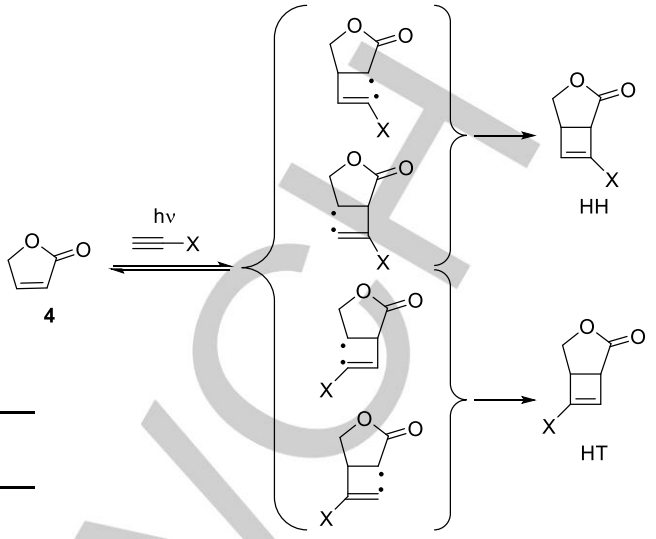
Table 2. Photoreaction of furanones **4** and **5** with alkynes **7**-**8**.[a]



Entry	Furanone	Alkyne	Solvent	Filter	Time [h]	Product (yield [%])[b]
1	**4**	**7**	CH_3CN	quartz	3	**16**(42),**18**(15)
2	**4**	**7**	acetone	pyrex	2	—
3	**4**	**8**	CH_3CN	quartz	6.5	**17**(22),**19**(15)
4	**4**	**8**	acetone	pyrex	2	—
5[c]	**5**	**7**	CH_3CN	quartz	3	**20**:**21**:**22**:**23**(49) 52:15:7:26 [d]
6	**5**	**8**	CH_3CN	quartz	2.5	—

[a] Irradiations were performed in a nitrogen saturated solution; the external cooling bath was at –40°C and the jacket cooling liquid at –15°C. The substrate conversion was monitored by GC. [b] Yield of isolated products. [c] 20% of the starting furanone **5** was recovered. [d] Product ratio determined by ^{1}H NMR.

We then turned out our attention to the photochemical reactivity of the same furanones towards the monosubstituted alkynes. The [2+2] cycloaddition of a simple furanone to an asymmetric alkyne may produce two regioisomers, the head-to-head (HH) and the head-to tail (HT) cycloadducts (Scheme 4). By parallelism to the extensive mechanistic studies on the photocycloaddition between cyclic enones and alkenes,[18] we can accept that 1,4-biradical intermediates are formed in similar ratio for both orientations, HH and HT, and that the regioselectivity of the reaction would be governed by the partitioning of these biradical intermediates between cyclization to afford a cyclobutene and fragmentation to revert to the starting materials. In several photocycloadditions involving unsymmetrical alkenes, a significant influence of the solvent polarity on the regioselectivity of the reaction has been found,[19] although a clear correlation has not been established. Therefore, it is interesting to evaluate the influence of the solvent polarity on the regioselectivity for every particular photocycloaddition.



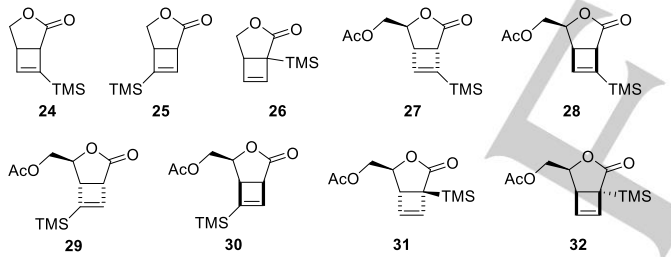
Scheme 4. Biradical intermediate species postulated for the [2+2] photocycloaddition of the simple furanone **4** to an asymmetric alkyne.

The photoreaction of **4** with trimethylsilylacetylene, **9**, may furnish the two isomeric primary cycloadducts **24** (HH) and **25** (HT) and the cyclobutene **26**, derived from the 1,3-acyl shift rearrangement of **25** (Table 3). The analogous rearrangement starting from the primary HH adduct **24** is degenerated. Thus, the irradiation of an acetonitrile solution of **4** and **9** furnished a mixture of the three expected products in 56% overall yield, wherein the primary HH adduct predominated (entry 1). The irradiation was stopped after 8.5 hours due to the increasing presence of byproducts and 25% of the starting furanone was recovered. By iterative column chromatography, samples enriched on each of the three isomers were isolated. The photoreaction performed in diethyl ether resulted in the formation of a complex crude mixture from where only the HH isomer **24** could be isolated in around 24% yield (entry 2), while the photosensitized reaction in acetone delivered a 61:39 mixture of the HH cycloadduct **24** and its HT isomer **25** in 20% global yield (entry 3). The presence of the rearranged isomer **26** was not detected.

Then, the photochemical reaction of the chiral lactone **5** with trimethylsilylacetylene was investigated. A priori this reaction could afford up to 6 isomeric cyclobutenes: *anti* HH, **27**, *syn* HH, **28**, *anti* HT, **29**, *syn* HT, **30**, *anti* rearranged, **31**, and *syn* rearranged, **32**. In practice, the irradiation in acetonitrile (entry 4) afforded a 30:36:6:28 mixture of the *anti* and *syn* HH cycloadducts, **27** and **28**, and the *anti* and *syn* rearranged derivatives, **31** and **32**, in 40% global yield, along with 35% of unreacted starting furanone. Repeated column chromatography allowed the isolation of a pure sample of **32** and enriched fractions of **27, 28** and **31** that made their characterization possible. The reaction was monitored by GC and, conversely to the parallel reaction of furanone **4**, signals from the primary HT cycloadducts were not detected. The steric interaction between the C-4 substitution and the TMS group in the HT isomers **29** and **30** may account for their fast conversion to the rearranged

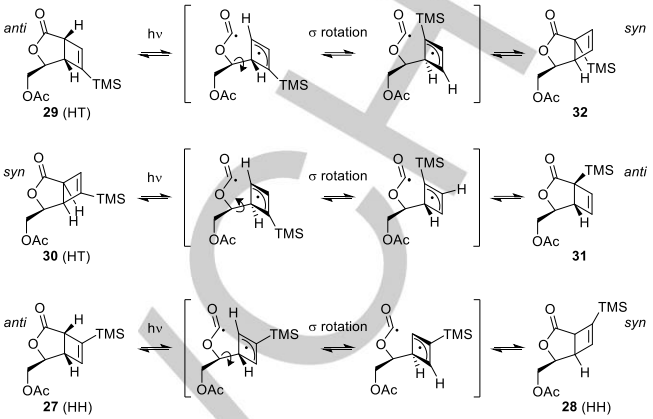
compounds **32** and **31**, respectively (Scheme 5). In the previously mentioned report of D'Annibale and co-workers on the photoreaction of other chiral 2(5*H*)-furanones to trialkylsilylacetylene in acetonitrile,[14] neither HT cycloadducts nor their rearranged derivatives were detected and, hence, the facial selectivity of the process was estimated as the ratio between the *syn* and *anti* primary adducts, concluding that the reaction was totally regioselective and the synfacial approach was preferred. However, an equilibrium may be established between the HH *syn* and *anti* primary adducts through an 1,3-acyl shift rearrangement similar to that observed by us for the HT isomers and, therefore, the product ratio cannot be taken as a reliable measure of the facial diastereoselectivity. When the photoreaction was performed in diethyl ether (entry 5), irradiation for 2.75 hours resulted in the formation of a complex crude mixture from where only the HH isomers **27** and **28** could be isolated, albeit in very poor yield. At shorter reaction times the HT isomers **29** and **30** were detected by GC analysis, but they evolved to unidentified products, among which the rearranged cyclobutenes **31** or **32** were not observed. The photosensitized reaction in acetone (entry 6) furnished a 31:34:18:17 mixture of cycloadducts **27-30** in 53% global yield, with 37% recovery of the starting furanone, and rearranged products were not detected.

Table 3. Photoreaction of furanones **4** and **5** with alkyne **9**.[a]



Entry	Furanone	Solvent	Filter	Time [h]	Product (yield [%])[b]
1[c]	**4**	CH_3CN	quartz	8.5	**24**:**25**:**26**(56) 58:15:27
2	**4**	Et_2O	quartz	3.5	**24** (≈24)
3	**4**	acetone	pyrex	5.5	**24**:**25** (20) 61:39
4[d]	**5**	CH_3CN	quartz	4	**27**:**28**:**31**:**32**(40) 30:36:6:28
5	**5**	Et_2O	quartz	2.75	**27**:**28**(12) 55:45
6[e]	**5**	acetone	pyrex	2	**27**:**28**:**29**:**30**(53) 31:34:18:17

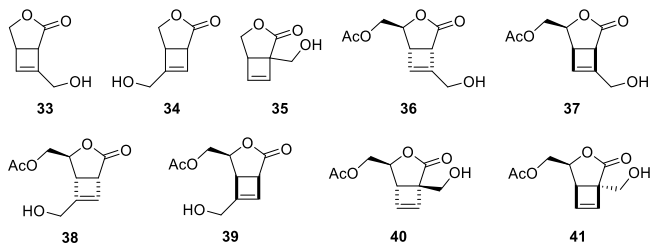
[a] Irradiations were performed in a nitrogen saturated solution; the external cooling bath was at –40°C and the jacket cooling liquid at –15°C. The substrate conversion was monitored by GC. [b] Product ratio determined by GC and ^{1}H NMR. [c] 25% of the starting furanone **4** was recovered. [d] 35% of the starting furanone **5** was recovered. [e] 37% of the starting furanone **5** was recovered.



Scheme 5. 1,3-Acyl shift rearrangements of the primary cycloadducts derived from furanone **5** and acetylene **9**.

Finally, the photoreactivity of lactones **4** and **5** with propargyl alcohol, **10**, was examined (Table 4). As above, some irradiations were stopped before complete consumption of the starting furanone to avoid the formation of large amounts of byproducts. The photoreaction of lactone **4** with alkyne **10** in acetonitrile (entry 1) provided a 57:29:14 mixture of the HH and HT primary cycloadducts, **33** and **34**, and the rearranged cyclobutene **35** in 66% global yield. Iterative column chromatography allowed the isolation of pure samples of the three isomers. The direct irradiation in diethyl ether (entry 2) and the photosensitized reaction in acetone (entry 3) produced very similar ratios of the primary cycloadducts in comparable yields, without evidences of the formation of the rearranged product. The photoreaction between the chiral furanone **5** and propargyl alcohol in acetonitrile (entry 4) afforded a 35:30:20:8:2:5 mixture of the *anti* and *syn* HH cycloadducts, **36** and **37**, the *anti* and *syn* HT cycloadducts, **38** and **39**, and the *anti* and *syn* rearranged cyclobutenes, **40** and **41**, in 60% overall yield. Iterative column chromatography allowed the isolation of pure samples of the primary HH cycloadduct **36** and the rearranged isomer **41**, whereas only enriched mixtures of the remaining isomers were obtained. Nevertheless, characterization of all isomers was achieved by ^{1}H and ^{13}C NMR. The reaction in diethyl ether (entry 5) afforded a 36:23:32:9 mixture of the primary cycloadducts **36**-**39** in 38% global yield and, although traces of the rearranged derivatives were detected by ^{1}H NMR of the crude product, their small proportion prevented their quantification. The photoreaction in acetone (entry 6) produced a mixture of the four primary cycloadducts in 49% total yield.

Table 4. Photoreaction of furanones **4** and **5** with alkyne **10**.[a]

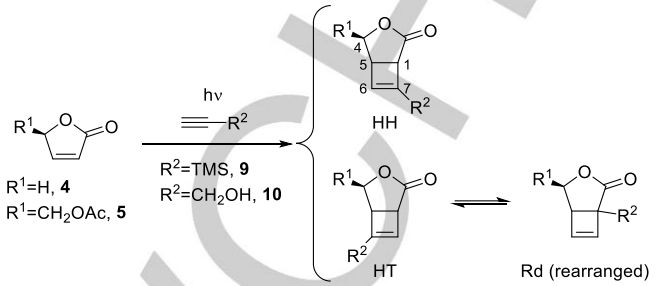


Entry	Furanone	Solvent	Filter	Time [h]	Product (yield [%])[b]
1[c]	**4**	CH_3CN	quartz	2.5	**33**:**34**:**35**(66) 57:29:14
2[d]	**4**	Et_2O	quartz	2.5	**33**:**34**(64) 58:42
3	**4**	acetone	pyrex	3	**33**:**34**(76) 58:42
4[e]	**5**	CH_3CN	quartz	1.5	**36**:**37**:**38**:**39**:**40**:**41**(60) 35:30:20:8:2:5
5	**5**	Et_2O	quartz	2	**36**:**37**:**38**:**39**(38) 36:23:32:9
6[f]	**5**	acetone	pyrex	2	**36**:**37**:**38**:**39**(49) 45:24:24:7

[a] Irradiations were performed in a nitrogen saturated solution; the external cooling bath was at –40°C and the jacket cooling liquid at –15°C. The substrate conversion was monitored by GC. [b] Product ratio determined by ^{1}H NMR. [c] 29% of the starting furanone **4** was recovered. [d] 17% of the starting furanone **4** was recovered. [e] 26% of the starting furanone **5** was recovered. [f] 29% of the starting furanone **5** was recovered.

Taking together the results of the photoreactions between furanones **4** and **5** and the monosubstituted alkynes **9** and **10**, the influence of the solvent on the regioselectivity can be evaluated. Since the 1,3-acyl shift rearrangement of the HH primary adducts does not produce constitutional isomers, the regioselectivity can be estimated as the ratio between the amount of the primary HH adducts and that of the primary HT adducts plus the rearranged cyclobutenes (Table 5). The connectivity of all the cyclobutenes was established with the help of HMQC and HMBC experiments, wherein a correlation between H-4 and the vinylic carbon atom C-6 is observed. The 1,3-acyl shift rearrangement occurs only in acetonitrile under direct irradiation, but not in the photosensitized reactions in acetone, an observation which is consistent with the idea that the singlet excited state S1 of the β,γ-unsaturated lactone is involved in the process. The results in diethyl ether are not considered, because the reactions in this solvent were not clean and the yields of identified products too low for being representative. The data summarized in Table 5 indicate that the solvent does not have a significant influence on the regioselectivity of the cycloaddition and that there is a moderate preference for the formation of HH adducts in all the cases, in agreement with previous observations on related reactions.[20]

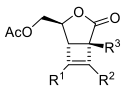
Table 5. Regioselectivity on the photoreaction of furanones **4** and **5** with alkynes **9** and **10**.



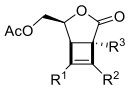
			CH_3CN		Acetone
Entry	Furanone	R^2	HH:HT:Rd	HH:(HT+Rd)	HH:HT
1	**4**	TMS	58:15:27	58:42	61:39
2	**4**	CH_2OH	57:29:14	57:43	67:33
3	**5**	TMS	66:-:34	66:34	65:35
4	**5**	CH_2OH	65:28:7	65:35	69:31

To assign the relative configuration of the cyclobutenes derived from the chiral furanone **5**, the value of the coupling constant $J_{4,5}$ was used as a reliable data. This value is expected to be smaller in the *anti* isomers (typically 1.0-2.5 Hz) compared to the *syn* isomers (typically 6.0-7.5 Hz). Table 6 collects the experimental values for $J_{4,5}$ of the synthesized cyclobutenes along with the chemical shift of C-1, which appears at lower field for the rearranged cycloadducts, where this carbon atom is a quaternary center. As expected, the effect is more pronounced in the hydroxymethyl compared to the TMS derivatives.

Table 6. Significant ^{1}H and ^{13}C NMR data for cyclobutenes derived from furanone **5**.[a]



Compound	R^1	R^2	R^3	$J_{4,5}$ (Hz)	C-1 (ppm)
13	H	TMS	TMS	2.2	52.4
20	CH_2OH	CH_2OH	H	1.6	44.4
22	H	CH_2OH	CH_2OH	1.6	58.8
27	H	TMS	H	2.0	47.8
29	TMS	H	H	1.5	47.6
31	H	H	TMS	1.4	51.4
36	H	CH_2OH	H	1.4	46.7
38	CH_2OH	H	H	1.5	44.0
40	H	H	CH_2OH	1.0	58.7



Compound	R^1	R^2	R^3	$J_{4,5}$ (Hz)	C-1 (ppm)
14	H	TMS	TMS	7.3	53.6
21	CH_2OH	CH_2OH	H	6.4	44.6
23	H	CH_2OH	CH_2OH	7.1	59.2
28	H	TMS	H	7.4	48.8
30	TMS	H	H	6.7	48.2
32	H	H	TMS	6.8	52.0
37	H	CH_2OH	H	7.5	47.0
39	CH_2OH	H	H	7.5	43.9
41	H	H	CH_2OH	7.0	59.6

[a] All the spectra were done in $CDCl_3$, except for **20** (acetone-d_6) and **21** (pyridine-d_5)

Conclusions

The photoreaction of 2(5*H*)-furanones with alkynes is an intricate process with a remarkable influence of multiple factors. When the reaction is performed in acetonitrile under direct excitation, in addition to the primary [2+2] cycloadducts, products derived from an 1,3-acyl shift rearrangement are also formed. For unsymmetrical alkynes, the regioselectivity of the cycloaddition has to be estimated taking into account that only the rearrangement of the head-to-tail primary adducts produces new regioisomers. Moreover, when the starting furanone is chiral, this rearrangement inverts the relative *anti/syn* geometry of the primary cycloadducts. In the reactions performed in acetone under photosensitized conditions, rearranged products were never detected, supporting that the 1,3-acyl shift takes place from the singlet excited state S_1 of the β,γ-unsaturated lactone. When bis(trimethylsilyl)acetylene was used as the alkyne partner, the primary adducts were not detected, most likely because they evolve fast to the less congested rearranged cyclobutenes, and, unexpectedly, the major photoproducts are monocyclic bis(trimethylsilyl)lactones. The complexity of these reactions prevents their synthetic application, but we have disclosed interesting mechanistic aspects that may serve to understand other similar forthcoming transformations.

Experimental Section

General Methods: Commercially available reagents were used as received. The solvents were dried by distillation over the appropriate drying agents. All reactions were performed avoiding moisture by standard procedures and under nitrogen atmosphere. Column chromatography was performed using silica gel (230-400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded at 250.13 and 62.5 MHz, 360.11 and 90.55 MHz, or 500.13 and 125.75 MHz. Proton and carbon chemical shifts are reported in ppm (δ) ($CDCl_3$, δ 7.26 for ^{1}H; $CDCl_3$, δ 77.2 for ^{13}C). NMR signals were assigned with the help of COSY, HSQC, HMBC, and NOESY experiments. Melting points were determined on hot stage and are uncorrected. Optical rotations were measured at 22 ± 2 °C.

General Procedure for the Photochemical Reactions. Irradiations were performed in a small conventional photochemical reactor (two-necked vessel fitted with a pyrex or quartz immersion type cooling jacket) using a high-pressure 125 W mercury lamp. Methanol at –15 °C was used for refrigeration of the immersion well jacket. The vessel was externally cooled at –40 °C with a dry ice-acetonitrile bath. The reaction mixtures were initially degassed by bubbling oxygen-free nitrogen through the solution for 10 min and then irradiated under atmosphere of nitrogen. The progress of the reactions was monitored by GC analysis of aliquot samples.

(1*RS*,5*RS*)-1,7-Bis(trimethylsilyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (11) and 3,4-bis(trimethylsilyl)dihydro-2(3*H*)-furanone (12). A solution of lactone **4** (119 mg, 1.40 mmol) and alkyne **6** (1.20 g, 7.04 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 6 h. Evaporation of the solvent and chromatographic purification of the residue (hexane-EtOAc 20:1) afforded some unreacted **4** (30 mg, 0.35 mmol, 25%), cyclobutene **11** (56 mg, 0.22 mmol, 16% yield) as a white solid, and lactone **12** (150 mg, 0.65 mmol, 47% yield) as a white solid.

When the irradiation was performed through a quartz filter in hexane (90 mL) for 6.5 h, from lactone **4** (119 mg, 1.40 mmol) and alkyne **6** (1.16 g, 6.81 mmol), after chromatographic purification of the crude material, the following fractions were obtained: (i) lactone **4** (81 mg, 0.35 mmol, 25%), (ii) cyclobutene **11** (23 mg, 0.09 mmol, 6% yield) and (iii) lactone **12** (81 mg, 0.35 mmol, 25% yield).

When the irradiation was performed through a quartz filter in diethyl ether (90 mL) for 3.5 h, from lactone **4** (119 mg, 1.40 mmol) and alkyne **6** (1.02 g, 5.98 mmol), after chromatographic purification of the crude material, the following fractions were obtained: (i) cyclobutene **11** (20 mg, 0.08 mmol, 6% yield) and (ii) lactone **12** (60 mg, 0.26 mmol, 19% yield).

11: Mp 62-65 ºC (from EtOAc-hexane); IR (ATR): υ = 3019, 2958, 2899, 2856, 1730, 1247, 1147, 833 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.78 (d, $^3J_{H,H}$ = 0.6 Hz, 1H, H-6), 4.23 (dd, $^2J_{H,H}$ = 9.7 Hz, $^3J_{H,H}$ = 2.0 Hz, 1H, H-4), 4.12 (dd, $^2J_{H,H}$ = 9.7 Hz, $^3J_{H,H}$ = 7.6 Hz, 1H, H-4), 3.42 (ddd, $^3J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 2.0 Hz, $^3J_{H,H}$ = 0.6 Hz, 1H, H-5), 0.18 (s, 9H, Si(CH_3)$_3$), 0.13 (s, 9H, Si(CH_3)$_3$); ^{13}CNMR (62.5 MHz, $CDCl_3$): δ = 177.2 (C=O, C-2), 163.3 (C, C-7), 150.4 (CH, C-6), 66.8 (CH_2, C-4), 52.1 (C, C-1), 46.1 (CH, C-5), –2.0 (CH_3, Si(CH_3)$_3$), –3.2 (CH_3, Si(CH_3)$_3$); elemental analysis calcd (%) for ($C_{12}H_{22}O_2Si_2$): C, 56.64; H, 8.71. Found: C, 57.02; H, 9.08.

12: Mp 31-35 ºC (from EtOAc-hexane); IR (ATR): υ = 2955, 2894, 2787, 1706, 1248, 1201, 1055, 833 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ= 4.39 (dd, $^2J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 1.3 Hz, 1H, H-5), 4.27 (ddd, $^2J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 1.7 Hz, $^4J_{H,H}$ = 0.7 Hz, 1H, H-5), 2.70 (dd, $^3J_{H,H}$ = 2.3 Hz, $^4J_{H,H}$ = 0.7 Hz, 1H, H-3), 2.25 (ddd, $^3J_{H,H}$ = 2.3, 1.7, 1.3 Hz, 1H, H-4), 0.18 (s, 9H, Si(CH_3)$_3$), 0.14 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 172.8 (C=O, C-2), 65.6 (CH_2, C-5), 36.2 (CH, C-4), 18.7 (CH, C-3), 0.0 (CH_3, Si(CH_3)$_3$), –1.3 (CH_3, Si(CH_3)$_3$).

(1*R*,4*S*,5*R*)- (13) and (1*S*,4*S*,5*S*)-4-acetyloxymethyl-1,7-bis(trimethylsilyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (14), and 5-acetyloxymethyl-3,4-bis(trimethylsilyl)dihydro-2(3*H*)-furanone (15). A solution of lactone **5** (240 mg, 1.54 mmol) and alkyne **6** (1.06 g, 6.22 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 4 h. GC and ^1H NMR analyses of the reaction mixture revealed the presence of four products in a ratio 56:16:16:11. Evaporation of the solvent and chromatographic purification of the residue (hexane-EtOAc 20:1) afforded unreacted **5** (70 mg, 0.45 mmol, 31%), a mixture of cyclobutenes **13** and **14** (66 mg, 0.20 mmol, 12% yield) as oil, and a mixture of two diastereomers of the bis(trimethylsilyl)lactones **15** (164 mg, 0.54 mmol, 35% yield) as a white solid. Repeated column chromatography (hexane to hexane-EtOAc 95:5) of the mixture of **15** provided one pure diastereomer, **15a**, as a white solid, and a fraction enriched in the other isomer, **15b.** Attempts to separate **13** from **14** were unsuccessful and fractions enriched in every isomer were analyzed.

13: IR (ATR): υ = 3023, 2956, 2898, 1743, 1250, 1045, 833, 748 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.81 (d, $^3J_{H,H}$ = 0.5 Hz, 1H, H-6), 4.56 (ddd, $^3J_{H,H}$ = 7.3, 5.1, 2.2 Hz, 1H, H-4), 4.11 (dd, $^2J_{H,H}$ = 11.7 Hz, $^3J_{H,H}$ = 5.1 Hz, 1H, H-8), 4.00 (dd, $^2J_{H,H}$ = 11.7 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, H-8), 3.11 (dd, $^3J_{H,H}$ = 2.2 Hz, $^3J_{H,H}$ = 0.5 Hz, 1H, H-5), 2.08 (s, 3H, CH_3CO), 0.20 (s, 9H, Si(CH_3)$_3$), 0.13 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.9 (C=O, C-2), 170.7 (C=O, CH_3*C*O), 163.4 (C, C-7), 150.2 (CH, C-6), 75.4 (CH, C-4), 65.4 (CH_2, C-8), 52.4 (C, C-1), 47.1 (CH, C-5), 20.8 (CH_3, *C*H_3CO), –1.9 (CH_3, Si(CH_3)$_3$), –3.0 (CH_3, Si(CH_3)$_3$); elemental analysis calcd (%) for ($C_{15}H_{26}O_4Si_2$): C, 55.17; H, 8.03. Found: C, 55.38; H, 8.43.

14: IR (ATR): υ = 2956, 2898, 1743, 1215, 1150, 832, 748 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.68 (d, $^3J_{H,H}$ = 0.7 Hz, 1H, H-6), 4.47 (ddd, $^3J_{H,H}$ = 7.9, 7.3, 4.1 Hz, 1H, H-4), 4.30 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, H-8), 4.21 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 7.9 Hz, 1H, H-8), 3.48 (dd, $^3J_{H,H}$ = 7.3, 0.7 Hz, 1H, H-5), 2.09 (s, 3H, CH_3CO), 0.19 (s, 9H, Si(CH_3)$_3$), 0.13 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.7 (C=O, C-2), 170.7 (C=O, CH_3*C*O), 164.6 (C, C-7), 146.9 (CH, C-6), 74.3 (CH, C-4), 64.2 (CH_2, C-8), 53.6 (C, C-1), 47.4 (CH, C-5), 20.8 (CH_3, *C*H_3CO), –1.9 (CH_3, Si(CH_3)$_3$), –3.2 (CH_3, Si(CH_3)$_3$); elemental analysis calcd (%) for ($C_{15}H_{26}O_4Si_2$): C, 55.17; H, 8.03. Found: C, 55.38; H, 8.43.

15a: mp: 48-51 ºC (EtOAc-hexane); $[\alpha]_D$ –57.8 (*c* 0.9, $CHCl_3$); IR (ATR): υ = 3083, 2953, 2902, 1740, 1702, 1237, 1198, 835, 754 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 4.53 (dddd, $^3J_{H,H}$ = 5.2, 4.7, 1.9 Hz, $^4J_{H,H}$ = 0.8 Hz, 1H, H-5), 4.21 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 5.2 Hz, 1H, H-6), 4.15 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 4.7 Hz, 1H, H-6), 2.69 (dd, $^3J_{H,H}$ = 2.1 Hz, $^4J_{H,H}$ = 0.8 Hz, 1H, H-3), 2.23 (dd, $^3J_{H,H}$ = 2.1, 1.9 Hz 1H, H-4), 2.08 (s, 3H, CH_3CO), 0.18 (s, 9H, Si(CH_3)$_3$), 0.14 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 172.2 (C=O, C-2), 170.7 (C=O, CH_3*C*O), 72.6 (CH, C-5), 66.0 (CH_2, C-6), 37.8 (CH, C-4), 20.8 (CH_3, *C*H_3CO), 18.5 (CH, C-3), 0.0 (CH_3, Si(CH_3)$_3$), -1.4 (CH_3, Si(CH_3)$_3$); elemental analysis calcd (%) for ($C_{13}H_{26}O_4Si_2$): C, 51.61; H, 8.66. Found: C, 51.67; H, 8.31.

15b: ^1H NMR (250 MHz, $CDCl_3$): δ = 4.60 (ddd, $^3J_{H,H}$ = 6.2, 5.9, 1.2 Hz, 1H, H-5), 4.30 (m, 2H, H-6), 2.76 (d, $^3J_{H,H}$ = 2.5 Hz, 1H, H-3), 2.32 (dd, $^3J_{H,H}$ = 2.5, 1.2 Hz, 1H, H-4), 2.09 (s, 3H, CH_3CO), 0.18 (s, 9H, Si(CH_3)$_3$), 0.16 (s, 9H, Si(CH_3)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 172.0 (C=O, C-2), 170.6 (C=O, CH_3*C*O), 72.1 (CH, C-5), 66.1 (CH_2, C-6), 38.3 (CH, C-4), 20.8 (CH_3, *C*H_3CO), 18.8 (CH, C-3), 0.2 (CH_3, Si(CH_3)$_3$), –1.3 (CH_3, Si(CH_3)$_3$).

(1*RS*,5*SR*)-6,7-Bis(hydroxymethyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (16) and (1*RS*,5*SR*)-1,7-bis(hydroxymethyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (18). A solution of lactone **4** (119 mg, 1.40 mmol) and alkyne **7** (650 mg, 7.55 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 3 h. Evaporation of the solvent and chromatographic purification of the residue (hexane–EtOAc 1:2) afforded **16** (100 mg, 0.59 mmol, 42% yield) as colorless oil and **18** (35 mg, 0.21 mmol, 15% yield) as colorless oil.

16: IR (ATR): υ = 3600-3000, 2974, 2916, 2860, 1733 cm^{-1}; ^1H NMR (250 MHz, acetone-d_6): δ = 4.49 (br s, 2H, OH), 4.34 (dd, $^2J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 2.1 Hz, 1H, H-4), 4.26 (m, 3H, H-4, H-9), 4.17 (d, $^2J_{H,H}$ = 15.7 Hz, 1H, H-8), 4.09 (d, $^2J_{H,H}$ = 15.7 Hz, 1H, H-8), 3.49 (m, 1H, H-5), 3.43 (m, 1H, H-1); ^{13}C NMR (62.5 MHz, acetone-d_6): δ = 174.9 (C=O, C-2), 145.6 (C, C-6), 142.2 (C, C-7), 67.7 (CH_2, C-4), 57.7 (CH_2, C-8), 57.4 (CH_2, C-9), 43.3 (CH, C-1), 39.1 (CH, C-5). HRMS (ESI^+): calcd for $[C_8H_{10}O_4+Na]^+$ 193.0471; found: 193.0477.

18: IR (ATR): υ = 3700-3000, 2923, 2852, 1741, 1634 cm^{-1}; ^1H NMR (250 MHz, acetone-d_6): δ = 6.22 (t, $^4J_{H,H}$ = 1.7, 1.7 Hz, 1H, H-6), 4.27 (dd, $^2J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 6.9 Hz, 1H, H-4), 4.15 (dd, $^2J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 1.8 Hz, 1H, H-4), 4.05 (d, $^2J_{H,H}$ = 11.3 Hz, 1H, H-8), 4.02 (m, 2H, H-9), 3.83 (d, J_{gem}=11.3 Hz, 1H, H-8), 3.41 (dd, $^3J_{H,H}$ = 6.9, 1.8 Hz, 1H, H-5), 2.89 (br s, 2H, OH); ^{13}C NMR (62.5 MHz, acetone-d_6): δ = 175.9 (C=O, C-2), 153.4 (C, C-7), 131.9 (CH, C-6), 67.9 (CH_2, C-4), 60.8 (CH_2, C-8), 59.0 (C, C-1), 57.8 (CH_2, C-9), 42.3 (CH, C-5). HRMS (ESI^+): calcd for $[C_8H_{10}O_4+Na]^+$ 193.0471; found: 193.0477.

(1*RS*,5*SR*)-6,7-Bis(acetyloxymethyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (17) and (1*RS*,5*SR*)-1,7-bis(acetyloxymethyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (19). A solution of lactone **4** (83 mg, 0.99 mmol) and alkyne **8** (800 mg, 4.70 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 6.5 h. Evaporation of the solvent and chromatographic purification of the residue (hexane–EtOAc 3:1) afforded **17** (50 mg, 0.21 mmol, 22% yield) as colorless oil and **19** (37 mg, 0.15 mmol, 15% yield) as a colorless oil.

17: IR (ATR): υ = 2970, 2922, 2852, 1769, 1733, 1171 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 4.80-4.60 (m, 4H, H-8, H-9), 4.37 (dd, $^2J_{H,H}$ = 10.0 Hz, $^3J_{H,H}$ = 2.2 Hz, 1H, H-4), 4.29 (dd, $^2J_{H,H}$ = 10.0 Hz, $^3J_{H,H}$ = 6.8 Hz, 1H, H-4), 3.56 (m, 1H, H-1), 3.51 (m, 1H, H-5), 2.09 (s, 6H, 2CH_3CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 173.9 (C=O, C-2), 170.7 (C=O, CH_3*C*O), 170.5 (C=O, CH_3*C*O), 142.9 (C, C-6), 141.0 (C, C-7), 67.4 (CH_2, C-4),

58.4/58.3 ($2CH_2$, C-8/C-9), 44.2 (CH, C-1), 39.9 (CH, C-5), 20.6 (CH_3, $2CH_3CO$). HRMS (ESI^+): calcd for $[C_{12}H_{14}O_6+Na]^+$ 277.0688; found: 277.0682.

19: IR (ATR): υ = 3068, 2966, 2908, 1762, 1734 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.30 (br s, 1H, H-6), 4.65 (dt, $^2J_{H,H}$ = 14.4 Hz, $^4J_{H,H}$ = 1.5, 1.5 Hz, 1H, H-8), 4.54 (d, $^2J_{H,H}$ = 11.7 Hz, 1H, H-9), 4.50 (dt, $^2J_{H,H}$ = 14.4 Hz, $^4J_{H,H}$ = 1.6,1.6 Hz, 1H, H-8), 4.43 (d, $^2J_{H,H}$ = 11.7 Hz, 1H, H-9), 4.30 (dd, $^2J_{H,H}$ = 9.9 Hz, $^3J_{H,H}$ = 6.9 Hz, 1H, H-4), 4.22 (dd, $^2J_{H,H}$ = 9.9 Hz, $^3J_{H,H}$ = 1.8 Hz, 1H, H-4), 3.42 (m, 1H, H-5), 2.08 (s, 3H, C*H*$_3$CO), 2.07 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 174.0 (C=O, C-2), 170.4 (C=O, CH_3CO), 170.3 (C=O, CH_3CO), 146.4 (C, C-7), 135.5 (CH, C-6), 67.3 (CH_2, C-4), 61.9 (CH_2, C-8), 58.9 (CH_2, C-9), 55.9 (C, C-1), 42.5 (CH, C-5), 20.7 (CH_3, *C*H$_3$CO), 20.6 (CH_3, *C*H$_3$CO). HRMS (ESI^+): calcd for $[C_{12}H_{14}O_6+Na]^+$ 277.0688; found: 277.0680.

(1*S*,4*S*,5*R*)- (20) and (1*R*,4*S*,5*S*)-4-acetyloxymethyl-6,7-bis(hydroxymethyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (21), (1*S*,4*S*,5*S*)- (22) and (1*R*,4*S*,5*R*)-4-acetyloxymethyl-1,7-bis(hydroxymethyl)-3-oxabicyclo[3.2.0]hept-6-en-2-one (23). A solution of lactone **5** (173 mg, 1.11 mmol) and alkyne **7** (453 mg, 5.26 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 3 h. Evaporation of the solvent and chromatographic purification of the residue (hexane–EtOAc 1:3) afforded a 52:15:24:7 mixture of **20**, **21**, **22** and **23** (132 mg, 0.55 mmol, 49% global yield) and some unreacted **5** (35 mg, 0.22 mmol, 20%). Repeated column chromatography (hexane–EtOAc 1:1 to 1:4) provided the following fractions: (i) an analytical sample of pure **20** as oil, (ii) an analytical sample of pure **23** as oil, (iii) a mixture of **20** and **21**, and (iv) a mixture of **22** and **23**. All attempts to separate **21** and **22** from **20** and **23**, respectively, were unsuccessful and fractions enriched in each isomer were analyzed.

20: $[\alpha]_D$ +56.0 (*c* 0.25, MeOH); ^1H NMR (250 MHz, $CDCl_3$): δ = 4.72 (m, 1H, H-4), 4.32 (m, 4H, H-9, H-10), 4.29 (dd, $^2J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 3.2 Hz, 1H, H-8), 4.20 (dd, $^2J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 3.9 Hz, 1H, H-8), 3.57 (m, 1H, H-1), 3.31 (m, 1H, H-5), 2.11 (s, 3H, C*H*$_3$CO); ^1H NMR (250 MHz, acetone-d_6): δ = 4.77 (dddd, $^3J_{H,H}$ = 4.4, 3.8, 1.5 Hz, $^4J_{H,H}$ = 0.5 Hz, 1H, H-4), 4.45 (m, 2H, OH), 4.28 (m, 2H, H-10), 4.24 (m, 1H, H-8), 4.20 (m, 1H, H-8), 4.14 (m, 2H, H-9), 3.51 (m, 1H, H-1), 3.36 (m, 1H, H-5), 2.03 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, acetone-d_6): δ = 174.5 (C=O, C-2), 170.3 (C=O, CH_3CO), 145.4 (C, C-6), 142.7 (C, C-7), 76.6 (CH, C-4), 66.2 (CH_2, C-8), 58.1 (CH_2, C-9), 57.8 (CH_2, C-10), 44.4 (CH, C-1), 41.7 (CH, C-5), 20.1 (CH_3, *C*H$_3$CO). HRMS (ESI^+): calcd for $[C_{11}H_{15}O_6+H]^+$ 243.0863; found 243.0857.

21: ^1H NMR (250 MHz, pyridine-d_5): δ = 6.34 (ddd, $^3J_{H,H}$ = 8.9, 6.7, 3.2 Hz, 1H, H-4), 6.05 (m, 4H, 2H-9, 2H-10), 5.91 (m, 2H, H-8), 5.17 (m, 1H, H-1), 5.12 (m, 1H, H-5), 3.46 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, pyridine-d_5): δ = 174.3 (C=O, C-2), 170.2 (C=O, CH_3CO), 144.5/143.8 (2C, C-6/C-7), 75.3 (CH, C-4), 64.9 (CH_2, C-8), 58.7/57.8 ($2CH_2$, C-9/C-10), 44.6 (CH, C-1), 40.8 (CH, C-5), 20.4 (CH_3, *C*H$_3$CO).

22: ^1H NMR (250 MHz, $CDCl_3$): δ = 6.28 (br s, 1H, H-6), 4.60 (ddd, $^3J_{H,H}$ = 3.6, 3.6, 1.4 Hz, 1H, H-4), 4.31 (m, 2H, H-8), 4.19-4.10 (m, 4H, H-9, H-10), 3.13 (d, $^3J_{H,H}$ = 1.4 Hz, 1H, H-5), 2.11 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.9 (C=O, C-2), 170.3 (C=O, CH_3CO), 152.2 (C, C-7), 132.6 (CH, C-6), 76.5 (CH, C-4), 65.4 (CH_2, C-8), 61.0 (CH_2, C-9), 58.8 (C, C-1), 58.2 (CH_2, C-10), 43.7 (CH, C-5), 20.7 (CH_3, *C*H$_3$CO).

23: $[\alpha]_D$ +42.2 (*c* 0.45, MeOH); IR (ATR): υ = 3650-3100, 2962, 2924, 2853, 1763, 1735 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.18 (br s, 1H, H-6), 4.63 (ddd, $^3J_{H,H}$ = 7.5, 6.8, 4.5 Hz, 1H, H-4), 4.23 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 4.5 Hz, 1H, H-8), 4.18 (dd, $^2J_{H,H}$ = 12.2 Hz, $^3J_{H,H}$ = 7.5 Hz, 1H, H-8), 4.11 (m, 2H, H-10), 4.06 (d, $^2J_{H,H}$ = 11.8 Hz, 1H, H-9), 3.93 (d, $^2J_{H,H}$ = 11.8 Hz, 1H, H-9), 3.35 (br d, $^3J_{H,H}$ = 6.8 Hz, 1H, H-5), 2.30 (br s, 2H, OH), 2.03 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.2 (C=O, C-2), 170.6 (C=O, CH_3CO), 152.8 (C, C-7), 130.1 (CH, C-6), 75.6 (CH, C-4), 63.2 (CH_2, C-8), 61.1 (CH_2, C-9), 59.2 (C, C-1), 58.3 (CH_2, C-10), 43.0 (CH, C-5), 20.7 (CH_3, *C*H$_3$CO). HRMS (ESI^+): calcd for $[C_{11}H_{15}O_6+H]^+$ 243.0863; found 243.0855.

(1*RS*,5*SR*)-7-Trimethylsilyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (24), (1*RS*,5*SR*)-6-trimethylsilyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (25) and (1*RS*,5*SR*)-1-trimethylsilyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (26). A solution of lactone **4** (119 mg, 1.40 mmol) and alkyne **9** (695 mg, 7.08 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 8.5 h. Evaporation of the solvent and chromatographic purification of the residue (hexane–EtOAc 6:1) afforded a 58:15:27 mixture of cyclobutenes **24**, **25** and **26** (128 mg, 0.70 mmol, 56% global yield) and some unreacted **4** (32 mg, 0.37 mmol, 25%). Repeated column chromatography (hexane–EtOAc 10:1 to 6:1) furnished enriched samples of **24**, **25** and **26** as colorless oils.

When the irradiation was performed through a quartz filter in diethyl ether (90 mL) for 3.5 h, from lactone **4** (119 mg, 1.40 mmol) and alkyne **9** (619 mg, 6.20 mmol), after chromatographic purification of the crude material, only **24** was detected (not totally pure, 60 mg, 0.33 mmol, ≈24% yield) was obtained.

When the irradiation was performed through a pyrex filter in acetone (90 mL) for 5.5 h, from lactone **4** (119 mg, 1.40 mmol) and alkyne **9** (691 mg, 7.03 mmol), after chromatographic purification of the crude material, a 61:39 mixture of **24** and **25** (51 mg, 0.28 mmol, 20% yield) was obtained.

24: IR (ATR): υ = 3027, 2958, 2900, 1756, 1161, 835, 757 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.73 (br s, 1H, H-6), 4.24 (m, 2H, H-4), 3.61 (m, 2H, H-1, H-5), 0.12 (s, 9H, Si(C*H*$_3$)$_3$); ^1H NMR (250 MHz, benzene-d_6) δ 6.21 (br s, 1H, H-6), 3.56 (dd, $^2J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 2.0 Hz, 1H, H-4), 3.43 (dd, $^2J_{H,H}$ = 9.6 Hz, $^3J_{H,H}$ = 7.5 Hz, 1H, H-4), 3.16 (d, $^3J_{H,H}$ = 3.6 Hz, 1H, H-1), 2.67 (ddd, $^3J_{H,H}$ = 7.5, 3.6, 2.0 Hz, 1H, H-5), 0.09 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, benzene-d_6): δ = 175.4 (C=O, C-2), 160.3 (C, C-7), 152.1 (CH, C-6), 67.9 (CH_2, C-4), 47.8 (CH, C-1), 43.0 (CH, C-5), -1.8 (CH_3, Si(*C*H$_3$)$_3$). HRMS (ESI^+): calcd for $[C_9H_{14}O_2Si+Na]^+$ 205.0661; found 205.0667.

25: IR (ATR): υ = 3032, 2958, 2901, 1760, 1163, 837, 756 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.70 (d, $^3J_{H,H}$ = 0.3 Hz, 1H, H-7), 4.34 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H, H-4), 4.23 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 2.1 Hz, 1H, H-4), 3.73 (br d, $^3J_{H,H}$ = 3.7 Hz, 1H, H-1), 3.56 (ddd, $^3J_{H,H}$ = 7.3, 3.7, 2.1 Hz, 1H, H-5), 0.14 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.6 (C=O, C-2), 161.5 (C, C-6), 148.0 (CH, C-7), 68.7 (CH_2, C-4), 47.4 (CH, C-1), 42.3 (CH, C-5), -2.1 (CH_3, Si(*C*H$_3$)$_3$). HRMS (ESI^+): calcd for $[C_9H_{14}O_2Si+Na]^+$ 205.0661; found 205.0663.

26: IR (ATR): υ = 3048, 2956, 2900, 1743, 1251, 1162, 835, 777 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.36 (d, $^3J_{H,H}$ = 2.5 Hz, 1H, H-6), 6.34 (d, $^3J_{H,H}$ = 2.5 Hz, 1H, H-7), 4.27 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 2.1 Hz, 1H, H-4), 4.17 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 7.4 Hz, 1H, H-4), 3.39 (dd, $^3J_{H,H}$ = 7.4, 2.1 Hz, 1H, H-5), 0.18 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 176.9 (C=O, C-2), 142.5 (CH, C-7), 139.6 (CH, C-6), 66.9 (CH_2, C-4), 50.7 (C, C-1), 45.2 (CH, C-5), -3.6 (CH_3, Si(*C*H$_3$)$_3$). HRMS (ESI^+): calcd for $[C_9H_{14}O_2Si+Na]^+$ 205.0661; found 205.0663.

(1*R*,4*S*,5*S*)- (27) and (1*S*,4*S*,5*R*)-4-acetyloxymethyl-7-trimethylsilyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (28), (1*R*,4*S*,5*S*)- (29) and (1*S*,4*S*,5*R*)-4-acetyloxymethyl-6-trimethylsilyl-3-

oxabicyclo[3.2.0]hept-6-en-2-one (30), (1*S*,4*S*,5*R*)- (31) and (1*R*,4*S*,5*S*)-4-acetyloxymethyl-1-trimethylsilyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (32). A solution of lactone **5** (214 mg, 1.37 mmol) and alkyne **9** (639 mg, 6.50 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 4 h. Evaporation of the solvent and chromatographic purification of the residue (hexane–EtOAc 5:1) afforded a 30:36:6:28 mixture of **27**, **28**, **31** and **32** (139 mg, 0.55 mmol, 40% global yield) and some unreacted **5** (75 mg, 0.48 mmol, 35%). Repeated column chromatography (hexane–EtOAc 16:1 to 10:1) furnished a pure sample of **32** and enriched fractions of **27**, **28** and **31** as colorless oils.

When the irradiation was performed through a quartz filter in diethyl ether (90 mL) for 2.75 h, from lactone **5** (207 mg, 1.33 mmol) and alkyne **9** (638 mg, 6.50 mmol), after chromatographic purification of the crude material, a 55:45 mixture of **27** and **28** (40 mg, 0.16 mmol, 12% yield) was obtained.

When the irradiation was performed through a pyrex filter in acetone (90 mL) for 2 h, from lactone **5** (162 mg, 1.04 mmol) and alkyne **9** (334 mg, 3.40 mmol), after chromatographic purification of the crude material, a 31:34:18:17 mixture of **27-30** (79 mg, 0.55 mmol, 53% global yield) and some unreacted lactone **5** (60 mg, 0.38 mmol, 37%) were obtained. All attempts to separate **29** and **30** from **27** and **28**, respectively, were unsuccessful, and fractions enriched in each isomer were analyzed.

27: IR (ATR): υ = 3030, 2956, 2896, 1776, 1742, 1161, 839, 757 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.72 (t, $^3J_{H,H}$ = 0.7, 0.7 Hz, 1H, H-6), 4.56 (dddd, $^3J_{H,H}$ = 4.1, 3.4, 1.6 Hz, $^4J_{H,H}$ = 0.7 Hz, 1H, H-4), 4.23 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 3.4 Hz, 1H, H-8), 4.12 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 4.1 Hz, 1H, H-8), 3.64 (dt, $^3J_{H,H}$ = 3.5 Hz, $^4J_{H,H}$ = 0.7, 0.7 Hz, 1H, H-1), 3.41 (ddd, $^3J_{H,H}$ = 3.5, 1.6, 0.7 Hz, 1H, H-5), 2.07 (s, 3H, C*H*$_3$CO), 0.13 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.2 (C=O, C-2), 170.5 (C=O, CH_3CO), 160.2 (C, C-7), 150.1 (CH, C-6), 76.2 (CH, C-4), 65.7 (CH_2, C-8), 47.8 (CH, C-1), 44.4 (CH, C-5), 20.7 (CH_3, *C*H$_3$CO), –2.5 (CH_3, Si(*C*H$_3$)$_3$). HRMS (ESI^+): calcd for $[C_{12}H_{18}O_4Si+Na]^+$ 277.0867; found 277.0862.

28: IR (ATR): υ = 3028, 2956, 2897, 1772, 1741, 1229, 1163, 837, 759 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.64 (t, $^3J_{H,H}$ = 0.7 Hz, $^4J_{H,H}$ = 0.7 Hz, 1H, H-6), 4.57 (dddd, $^3J_{H,H}$ = 7.6, 6.4, 4.3 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, H-4), 4.29 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 4.3 Hz, 1H, H-8), 4.21 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 7.6 Hz, 1H, H-8), 3.65 (m, 2H, H-1, H-5), 2.08 (s, 3H, C*H*$_3$CO), 0.11 (s, 9H, Si(C*H*$_3$)$_3$); ^1H NMR (250 MHz, benzene-*d*$_6$): δ = 6.11 (dd, $^3J_{H,H}$ = 0.6 Hz, $^4J_{H,H}$ = 0.5 Hz, 1H, H-6), 3.98 (m, 3H, H-4, H-8), 3.15 (ddd, $^3J_{H,H}$ = 3.5 Hz, $^4J_{H,H}$ = 0.8, 0.5 Hz, 1H, H-1), 2.78 (ddd, $^3J_{H,H}$ = 6.1, 3.5, 0.6 Hz, 1H, H-5), 1.64 (s, 3H, C*H*$_3$CO), 0.06 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, benzene-*d*$_6$): δ = 174.0 (C=O, C-2), 170.4 (C=O, CH_3CO), 161.4 (C, C-7), 148.7 (CH, C-6), 75.7 (CH, C-4), 64.5 (CH_2, C-8), 48.8 (CH, C-1), 44.3 (CH, C-5), 20.7 (CH_3, *C*H$_3$CO), -1.9 (CH_3, Si(*C*H$_3$)$_3$). HRMS (ESI^+): calcd for $[C_{12}H_{18}O_4Si+Na]^+$ 277.0867; found 277.0862.

29: ^1H NMR (250 MHz, $CDCl_3$): δ = 6.60 (d, $^3J_{H,H}$ = 0.7 Hz, 1H, H-7), 4.52 (m, 1H, H-4), 4.25 (m, 2H, H-8), 3.75 (ddd, $^3J_{H,H}$ = 3.5, 0.7 Hz, $^4J_{H,H}$ = 0.7 Hz, 1H, H-1), 3.33 (dd, $^3J_{H,H}$ = 3.5, 1.6 Hz, 1H, H-5), 2.08 (s, 3H, C*H*$_3$CO), 0.12 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 174.5 (C=O, C-2), 170.2 (C=O, CH_3CO), 160.6 (C, C-6), 147.7 (CH, C-7), 76.7 (CH, C-4), 65.4 (CH_2, C-8), 47.6 (CH, C-1), 44.2 (CH, C-5), 20.4 (CH_3, *C*H$_3$CO), -2.8 (CH_3, Si(*C*H$_3$)$_3$).

30: ^1H NMR (250 MHz, $CDCl_3$): δ = 6.79 (d, $^3J_{H,H}$ = 0.9 Hz, 1H, H-7), 4.77 (ddd, $^3J_{H,H}$ = 7.1, 4.7, 3.5 Hz, 1H, H-4), 4.17 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 3.5 Hz, 1H, H-8), 4.09 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 4.7 Hz, 1H, H-8), 3.81 (dd, $^3J_{H,H}$ = 3.7, 0.9 Hz, 1H, H-1), 3.65 (dd, $^3J_{H,H}$ = 7.1, 3.7 Hz, 1H, H-5), 2.09 (s, 3H, C*H*$_3$CO), 0.08 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 179.7 (C=O, C-2), 170.7 (C=O, CH_3CO), 158.9 (C, C-6), 150.4 (CH, C-7), 76.1 (CH, C-4), 64.5 (CH_2, C-8), 48.2 (CH, C-1), 44.0 (CH, C-5), 20.7 (CH_3, *C*H$_3$CO), -1.9 (CH_3, Si(*C*H$_3$)$_3$).

31: ^1H NMR (250 MHz, $CDCl_3$): δ = 6.40 (dd, $^3J_{H,H}$ = 2.6, 0.5 Hz, 1H, H-6), 6.35 (dd, $^3J_{H,H}$ = 2.6 Hz, $^4J_{H,H}$ = 0.5 Hz, 1H, H-7), 4.62 (ddd, $^3J_{H,H}$ = 6.5, 4.8, 2.0 Hz, 1H, H-4), 4.16 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 4.8 Hz, 1H, H-8), 4.04 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 6.5 Hz, 1H, H-8), 3.13 (ddd, $^3J_{H,H}$ = 2.0, 0.5 Hz, $^4J_{H,H}$ = 0.5 Hz, 1H, H-5), 2.12 (s, 3H, C*H*$_3$CO), 0.21 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.7 (C=O, C-2), 170.7 (C=O, CH_3CO), 142.5 (CH, C-7), 139.1 (CH, C-6), 75.2 (CH, C-4), 65.4 (CH_2, C-8), 51.4 (C, C-1), 46.6 (CH, C-5), 20.8 (CH_3, *C*H$_3$CO), -3.5 (CH_3, Si(*C*H$_3$)$_3$).

32: $[\alpha]_D$ +40.0 (*c* 0.9, $CHCl_3$); IR (ATR): υ = 3050, 2955, 2898, 1742, 1244, 1230, 1165, 1114, 839, 757 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.37 (d, $^3J_{H,H}$ = 2.6 Hz, 1H, H-7), 6.27 (dd, $^3J_{H,H}$ = 2.6, 0.7 Hz, 1H, H-6), 4.53 (ddd, $^3J_{H,H}$ = 7.7, 7.7, 4.2 Hz, 1H, H-4), 4.32 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 4.2 Hz, 1H, H-8), 4.23 (dd, $^2J_{H,H}$ = 11.9 Hz, $^3J_{H,H}$ = 7.7 Hz, 1H, H-8), 3.46 (dd, $^3J_{H,H}$ = 7.7, 0.7 Hz, 1H, H-5), 2.09 (s, 3H, C*H*$_3$CO), 0.18 (s, 9H, Si(C*H*$_3$)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.4 (C=O, C-2), 170.7 (C=O, CH_3CO), 143.2 (CH, C-7), 136.3 (CH, C-6), 74.2 (CH, C-4), 64.0 (CH_2, C-8), 52.0 (C, C-1), 46.6 (CH, C-5), 20.7 (CH_3, *C*H$_3$CO), –3.7 (CH_3, Si(*C*H$_3$)$_3$). HRMS (ESI^+): calcd for $[C_{12}H_{18}O_4Si+Na]^+$ 277.0867; found 277.0860.

(1*RS*,5*RS*)-7-Hydroxymethyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (33), (1*RS*,5*RS*)-6-hydroxymethyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (34) and (1*RS*,5*SR*)-1-hydroxymethyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (35). A solution of lactone **4** (119 mg, 1.40 mmol) and alkyne **10** (385 mg, 6.89 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 2.5 h at. Evaporation of the solvent and chromatographic purification of the residue (hexane-EtOAc 2:1) afforded a 57:29:14 mixture of **33**, **34** and **35** (130 mg, 0.93 mmol, 66% global yield) and some unreacted **4** (35 mg, 0.42 mmol, 29%). Repeated column chromatography (hexane–EtOAc 3:1 to 1:1) furnished analytical samples of **33** and **35** as colorless oils.

When the irradiation was performed through a quartz filter in diethyl ether (90 mL) for 2.5 h, from lactone **4** (119 mg, 1.40 mmol) and alkyne **10** (392 mg, 7.00 mmol), after chromatographic purification of the crude material, a 58:42 mixture of **33** and **34** (127 mg, 0.90 mmol, 64% global yield) and some unreacted lactone **4** (20 mg, 0.24 mmol, 17%) were obtained.

When the irradiation was performed through a pyrex filter in acetone (90 mL) for 3 h, from lactone **4** (119 mg, 1.40 mmol) and alkyne **10** (392 mg, 7.00 mmol), after chromatographic purification of the crude material, a 67:33 mixture of **33** and **34** (149 mg, 1.06 mmol, 76% yield) was obtained.

33: IR (ATR): υ = 3700-3000, 2973, 2920, 2855, 1718, 1376, 1170 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.19 (br s, 1H, H-6), 4.32 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 7.0 Hz, 1H, H-4), 4.25 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 2.2 Hz, 1H, H-4), 4.18 (m, 2H, H-8), 3.65 (br d, $^3J_{H,H}$ = 3.7 Hz, 1H, H-1), 3.47 (dddd, $^3J_{H,H}$ = 7.0, 3.7, 2.2, 0.5 Hz, 1H, H-5), 2.22 (br s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.6 (C=O, C-2), 150.7 (C, C-7), 132.5 (CH, C-6), 69.2 (CH_2, C-4), 59.3 (CH_2, C-8), 46.0 (CH, C-1), 38.5 (CH, C-5). HRMS (ESI^+) calcd for $[C_7H_8O_3+Na]^+$ 163.0366; found 163.0364.

34: IR (ATR): υ = 3600-3000, 2976, 2918, 2856, 1716, 1165 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 6.18 (br s, 1H, H-7), 4.41 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 2.1 Hz, 1H, H-4), 4.31 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, H-4),

4.24 (m, 2H, H-8), 3.65 (m, 1H, H-5), 3.53 (m, 1H, H-1), 2.0 (br s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.7 (C=O, C-2), 153.3 (C, C-6), 130.4 (CH, C-7), 67.2 (CH_2, C-4), 59.2 (CH_2, C-8), 43.2 (CH, C-1), 41.3 (CH, C-5).

35: IR (ATR): υ = 3600-3100, 3056, 2974, 2913, 2875, 1753, 1176 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.46 (d, $^3J_{H,H}$ = 2.7 Hz, 1H, H-6), 6.29 (d, $^3J_{H,H}$ = 2.7 Hz, 1H, H-7), 4.33 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 7.2 Hz, 1H, H-4), 4.24 (dd, $^2J_{H,H}$ = 9.8 Hz, $^3J_{H,H}$ = 2.1 Hz, 1H, H-4), 4.10 (d, $^2J_{H,H}$ = 11.4 Hz, H-8), 3.92 (d, $^2J_{H,H}$ = 11.4 Hz, 1H, H-8), 3.49 (dd, $^3J_{H,H}$ = 7.2, 2.1 Hz, 1H, H-5), 2.22 (br s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 176.9 (C=O, C-2), 141.5 (CH, C-6), 139.9 (CH, C-7), 67.3 (CH_2, C-4), 62.0 (CH_2, C-8), 58.3 (C, C-1), 44.5 (CH, C-5). HRMS (ESI$^+$) calcd for $[C_7H_8O_3+Na]^+$ 163.0366; found 163.0368.

(1*S*,4*S*,5*S*)- (36) and (1R,4S,5R)-4-acetyloxymethyl-7-hydroxymethyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (37), (1*R*,4*S*,5*R*)- (38) and (1*S*,4*S*,5*S*)-4-acetyloxymethyl-6-hydroxymethyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (39), (1*R*,4*S*,5*S*)- (40) and (1S,4S,5R)-4-acetyloxymethyl-1-hydroxymethyl-3-oxabicyclo[3.2.0]hept-6-en-2-one (41). A solution of lactone **5** (170 mg, 1.09 mmol) and alkyne **10** (337 mg, 6.01 mmol) in acetonitrile (90 mL) was irradiated through a quartz filter for 1.5 h. Evaporation of the solvent and chromatographic purification of the residue (hexane–EtOAc 1:1) afforded a 35:30:20:8:2:5 mixture of **36**, **37**, **38**, **39**, **40** and **41** (135 mg, 0.64 mmol, 60% global yield) and some unreacted **5** (45 mg, 0.29 mmol, 26%). Repeated column chromatography (hexane–EtOAc from 2:1 to 1:2) provided the following fractions: (i) an analytical sample of **36** as oil, (ii) an analytical sample of **40** as oil, (iii) an analytical sample of **41** as oil (iv) a mixture of **36** and **37** and (v) a mixture of **38** and **39**. All attempts to separate **37** and **38** from **36** and **39**, respectively, were unsuccessful and fractions enriched in each isomer were analyzed.

When the irradiation was performed through a quartz filter in diethyl ether (90 mL) for 2 h, from lactone **5** (150 mg, 0.97 mmol) and alkyne **10** (337 mg, 6.01 mmol), after chromatographic purification of the crude material, a 36:23:32:9 mixture of **36-39** (78 mg, 0.37 mmol, 38% global yield) was obtained.

When the irradiation was performed through a pyrex filter in acetone (90 mL) for 2 h, from lactone **5** (170 mg, 1.09 mmol) and alkyne **10** (337 mg, 6.01 mmol), after chromatographic purification of the crude material, a 45:24:24:7 mixture of **36-39** (110 mg, 0.52 mmol, 49% global yield) and some unreacted **5** (50 mg, 0.32 mmol, 29%) were obtained.

36: $[\alpha]_D$ –56.2 (*c* 1.05, MeOH); IR (ATR): υ = 3550-3100, 3020, 2964, 2924, 2854, 1769, 1737 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.21 (m, 1H, H-6), 4.60 (ddd, $^3J_{H,H}$ = 4.2, 3.3, 1.4 Hz, 1H, H-4), 4.26 (dd, $^2J_{H,H}$ = 12.1 Hz, $^3J_{H,H}$ = 3.3 Hz, 1H, H-8), 4.19 (m, 2H, H-9), 4.16 (dd, $^2J_{H,H}$ = 12.1 Hz, $^3J_{H,H}$ = 4.2 Hz, 1H, H-8), 3.70 (dd, $^3J_{H,H}$ = 3.5 Hz, $^4J_{H,H}$ = 0.4 Hz, 1H, H-1), 3.30 (m, 1H, H-5), 2.08 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 174.7 (C=O, C-2), 170.5 (C=O, CH_3CO), 150.8 (C, C-7), 131.7 (CH, C-6), 77.1 (CH, C-4), 65.6 (CH_2, C-8), 59.3 (CH_2, C-9), 46.7 (CH, C-1), 40.8 (CH, C-5), 20.6 (CH_3, *C*H_3CO). HRMS (ESI$^+$): calcd for $[C_{10}H_{13}O_5+H]^+$ 213.0760; found: 213.0757.

37: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.13 (m, 1H, H-6), 4.67 (ddd, $^3J_{H,H}$ = 7.5, 4.5, 2.3 Hz, 1H, H-4), 4.20 (m, 4H, H-8, H-9), 3.74 (dd, $^3J_{H,H}$ = 3.6 Hz, $^4J_{H,H}$ = 1.0 Hz, 1H, H-1), 3.57 (m, 1H, H-5), 2.10 (s, 3H, C*H*$_3$CO), 1.95 (br s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 173.9 (C=O, C-2), 170.6 (C=O, CH_3CO), 151.5 (C, C-7), 129.2 (CH, C-6), 76.3 (CH, C-4), 65.7 (CH_2, C-8), 63.3 (CH_2, C-9), 47.0 (CH, C-1), 40.1 (CH, C-5), 20.7 (CH_3, *C*H_3CO).

38: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.17 (br s, 1H, H-7), 4.74 (ddd, $^3J_{H,H}$ = 4.0, 3.6, 1.5 Hz, 1H, H-4), 4.29 (dd, $^2J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 4.0 Hz, 1H, H-8), 4.23 (m, 2H, H-9), 4.20 (m, 1H, H-8), 3.56 (m, 1H, H-1), 3.43 (m, 1H, H-5), 2.08 (s, 3H, C*H*$_3$CO), 1.70 (br s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 174.8 (C=O, C-2), 170.5 (C=O, CH_3CO), 152.5 (C, C-6), 130.7 (CH, C-7), 75.4 (CH, C-4), 65.7 (CH_2, C-8), 59.3 (CH_2, C-9), 44.0 (CH, C-1), 43.7 (CH, C-5), 20.7 (CH_3, *C*H_3CO).

39: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.25 (br s, 1H, H-7), 4.66 (ddd, $^3J_{H,H}$ = 7.5, 4.4, 3.8 Hz, 1H, H-4), 4.22 (m, 4H, H-8, H-9), 3.68 (m, 1H, H-1), 3.59 (m, 1H, H-5), 2.09 (s, 3H, C*H*$_3$CO), 1.75 (br s, 1H, OH); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 173.4 (C=O, C-2), 170.6 (C=O, CH_3CO), 151.0 (C, C-6), 131.7 (CH, C-7), 75.7 (CH, C-4), 63.9 (CH_2, C-8), 63.3 (CH_2, C-9), 43.9 (CH, C-1), 42.3 (CH, C-5), 20.7 (CH_3, CH_3CO).

40: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.47 (d, $^3J_{H,H}$ = 2.7 Hz, 1H, H-6), 6.34 (d, $^3J_{H,H}$ = 2.7 Hz, 1H, H-7), 4.59 (ddd, $^3J_{H,H}$ = 5.1, 3.9, 1.0 Hz, 1H, H-4), 4.24 (dd, $^2J_{H,H}$ = 12.1 Hz, $^3J_{H,H}$ = 3.9 Hz, 1H, H-8), 4.16 (dd, $^2J_{H,H}$ = 12.1 Hz, $^3J_{H,H}$ = 5.1 Hz, 1H, H-8), 4.07 (d, $^2J_{H,H}$ = 11.4 Hz, H-9), 3.95 (d, $^2J_{H,H}$ = 11.4 Hz, 1H, H-9), 3.24 (d, $^3J_{H,H}$ = 1.0 Hz, 1H, H-5), 2.10 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.8 (C=O, C-2), 170.5 (C=O, CH_3CO), 140.7 (CH, C-6), 140.4 (CH, C-7), 75.4 (CH, C-4), 65.3 (CH_2, C-8), 61.7 (CH_2, C-9), 58.7 (C, C-1), 46.3 (CH, C-5), 20.7 (CH_3, *C*H_3CO). HRMS (ESI$^+$): calcd for $[C_{10}H_{13}O_5+Na]^+$ 235.0577; found 235.0572.

41: IR (ATR): υ = 3700-3100, 3059, 2960, 2923, 2852, 1768, 1735, 1178 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 6.40 (dd, $^3J_{H,H}$ = 2.8, 0.5 Hz, 1H, H-6), 6.33 (d, $^3J_{H,H}$ = 2.8 Hz, 1H, H-7), 4.67 (ddd, $^3J_{H,H}$ = 7.5, 7.0, 4.5 Hz, 1H, H-4), 4.32 (dd, $^2J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 4.5 Hz, 1H, H-8), 4.23 (dd, $^2J_{H,H}$ = 12.0 Hz, $^3J_{H,H}$ = 7.5 Hz, 1H, H-8), 4.13 (d, $^2J_{H,H}$ = 11.4 Hz, H-9), 3.91 (d, $^2J_{H,H}$ = 11.4 Hz, 1H, H-9), 3.55 (dd, $^3J_{H,H}$ = 7.0, 0.5 Hz, 1H, H-5), 2.10 (s, 3H, C*H*$_3$CO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 175.3 (C=O, C-2), 170.6 (C=O, CH_3CO), 140.7 (CH, C-7), 138.5 (CH, C-6), 74.6 (CH, C-4), 63.3 (CH_2, C-8), 61.9 (CH_2, C-9), 59.6 (C, C-1), 46.0 (CH, C-5), 20.7 (CH_3, *C*H_3CO). HRMS (ESI$^+$): calcd for $[C_{10}H_{13}O_5+Na]^+$ 235.0577; found 235.0575.

Supporting Information: ^{1}H and ^{13}C NMR spectra of all new compounds and 2D NMR spectra for compounds **12**, **14**,**15a**. **16-20**, **23-28**, **32-36** and **41**.

Acknowledgements

We acknowledge the Spanish Dirección General de Investigación for financial support (projects CTQ2010-15380 and CTQ2013-41161-R) and Ministerio de Educación y Ciencia for a grant (to R. F.).

Keywords: 2(5*H*)-furanones • alkynes • photoreaction • regioselectivity • stereoselectivity

[1] More than 1600 cyclobutane-containing natural products have been reported to date. T. P. Yoon, *ACS Catal.* **2013**, *3*, 895–902.

[2] Y. J. Hong, D. J. Tantillo, *Chem. Soc. Rev.* **2014**, *43*, 5042–5050.

[3] a) A. Sergeiko, V. V. Poroikov, L. O. Hanu, V. M. Dembitsky, *Open Med. Chem. J.* **2008**, *2,* 26–37; b) V. M. Dembitsky, *J. Nat. Med.* **2008,** *62*, 1–33; c) V. M. Dembitsky, *Phytomedicine* **2014**, *21*, 1559–1581.

[4] A. Ebead, R. Fournier, E. Lee-Ruff, *Nucleos. Nucleot. Nucl.* **2011**, *30*, 391–404, and references therein.

[5] For a recent review on this topic see: T. Seiser, T. Saget, D. N. Tran, N. Cramer, *Angew. Chem. Int. Ed.* **2011**, *50*, 7740–7752.

[6] a) J. C. Namyslo, D. E. Kaufmann, *Chem. Rev.* **2003**, *103*, 1485–1538; b) E. Lee-Ruff, G. Mladenova, *Chem. Rev.* **2003**, *103*, 1449–1484; c) Y. Xu, M. L. Conner, M. K. Brown, *Angew. Chem. Int. Ed.* **2015**, *54*, 11918-11928.

[7] a) Gauvry, N.; Lescop, C.; Huet, F. *Eur. J. Org. Chem.* **2006**, 5207–5218; b) C. Souris, A. Misale, Y. Chen, M. Luparia, N. Maulide, *Org. Lett.* **2015**, *17*, 4486–4489.

[8] a) J. Iriondo-Alberdi, M. F. Greaney, *Eur. J. Org. Chem.* **2007**, 4801−4815; c) N. Hoffmann, *Chem. Rev.* **2008**, *108*, 1052−1103; c) T. Bach, J. P. Hehn, *Angew. Chem. Int. Ed.* **2011**, *50*, 1000−1045.

[9] D. I. Schuster, G. Lem, N. A. Kaprinidis, *Chem. Rev.* **1993**, *93*, 3–22.

[10] a) P. de March, M. Figueredo, J. Font, J. Raya, A. Alvarez-Larena, J. F. Piniella, *J. Org. Chem.* **2003**, *68*, 2437–2447; b) A. Rustullet, R. Alibés, P. de March, M. Figueredo, J. Font, *Org. Lett.* **2007**, *9*, 2827–2830; c) M. Racamonde, R.Alibés, M. Figueredo, J. Font, P. de March, *J. Org. Chem.* **2008**, *73*, *5944–5952*; d) R. Flores, A. Rustullet, R. Alibés, A. Álvarez-Larena, P. de March, M. Figueredo, J. Font, *J. Org. Chem***. 2011**, *76*, 5369–5383; e) S. Parés,; R. Alibés, M. Figueredo, J. Font, T. Parella, *Eur. J. Org. Chem.* **2012**, 1404–1417; f) R. Miralles-Llumà,; A. Figueras, F. Busqué, A. Alvarez-Larena, J. Balzarini, M. Figueredo, J. Font, R. Alibés, J.-D. Maréchal, *Eur. J. Org. Chem.* **2013**, 7761–7775; g) L. Pérez, R. Alibés; P. De March; F. Busqué; M. Figueredo; J. Font *J. Org. Chem.* **2013**, *78*, 4483-4489.

[11] R. Alibés, P. de March, M. Figueredo, J. Font, X. Fu, M. Racamonde, A. Álvarez-Larena, J. F. Piniella, *J. Org. Chem.* **2003**, *68*, 1283–1289.

[12] a) K. N. Houk, *Chem. Rev.* **1976**, *76*, 1–74; b) Ninomiya, I.; Naito, T. *Photochemical Synthesis;* Academic Press; London; **1989**, chapter 6, p.79.

[13] R. Alibés, P. de March, M. Figueredo, J. Font, M. Racamonde, A. Rustullet, A. Alvarez-Larena, J. F. Piniella, T. Parella, *Tetrahedron Lett.* **2003**, *44*, 69–71.

[14] A. D'Annibale, M. D'Auria, G. Mancini, A. D. Pace, R. Racioppi, *Eur. J. Org. Chem.* **2012**, 785–791.

[15] L. Birkofer, D. Eichstädt, *J. Organomet. Chem.* **1978**, *145*, C29–C30.

[16] P. E. Eaton, *Tetrahedron Lett.* **1964**, 3695–3698.

[17] a) A. Padwa, L. Zhi, G. E. Fryxell, *J. Org. Chem.* **1991**, *56*, 1077–1083; b) V. Singh, *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Lenci, F., Eds.; CRC: Boca Raton, FL; **2004**, chapter 79.

[18] a) P. G. Bauslaugh, *Synthesis* **1970**, 287–300; b) D. J. Hastings, A. C. Weedon, *J. Am. Chem. Soc.* **1991**, *113*, 8525–8527; c) D. Andrew, D. J. Hastings, D. L. Oldroyd, A. Rudolph, A. C. Weedon, D. F. Wong, B. Zhang, *Pure & Appl. Chem.* **1992**, *64*, 1327–1334; d) D. Andrew, A. C. Weedon, *J. Am. Chem. Soc.* **1995**, *117*, 5647–5663.

[19] a) B. D. Challand, P. de Mayo, *Chem. Comm.* **1968**, 982–983; b) R. O. Loufty, P. de Mayo, *Can. J. Chem.* **1972**, *50*, 3465–3471; c) N. Berenjian, P. de Mayo, M.-E. Sturgeon, L. K. Sydnes, A. C. Weedon, *Can. J. Chem.* **1982**, *60*, 425–436.

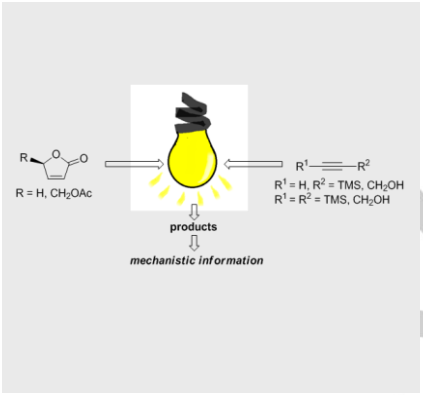
[20] a) E. P. Serebryakov, K. Ya. Burstein, *Tetrahedron* **1978**, *34*, 3233–3238; b) E. P. Serebryakov, S. D. Kulomzina-Pletneva, A. Kh. Margaryan, *Tetrahedron* **1979**, *35*, 77–86; c) A. A. Avetisyan, A. Kh.; Margaryan, G. K. Nalbandyan, T. V. Avetisyan, *Zhum. Org. Khim.* **1989**, *25*, 530–536; d) J. Soulie, M. J. Pouet, *Tetrahedron* **1978**, *33*, 2521–2525.

Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

The photoreaction of 2(5*H*)-furanones with substituted alkynes was investigated. Some interesting mechanistic aspects are unveiled.



Ramon Flores, Josep Font, Ramon Alibés, and Marta Figueredo**

Page No. – Page No.
A Study on the Photoreaction of 2(5*H*)-Furanones with Substituted Acetylenes: Evidences for a Mechanistic Reformulation

Layout 2:

FULL PAPER

((Insert TOC Graphic here; max. width: 11.5 cm; max. height: 2.5 cm))

*Author(s), Corresponding Author(s)**

Page No. – Page No.

Title

Text for Table of Contents