Regioselectivity of the Intramolecular Photocycloaddition of α,β-Butenolides to a Terminal Alkene

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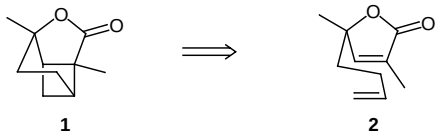
Abstract: The intramolecular [2+2] photocycloaddition of α,β-butenolides to a terminal double bond tethered to the lactone through the γ-position and located at a suitable distance has been studied. The regioselectivity of the photoisomerization depends on the substitution pattern of the substrate and can be rationalized by simple theoretical calculations performed on the diradical intermediates.

Key words: intramolecular photochemical cycloaddition, α,β-butenolides, alkenes, regioselectivity, intermediate diradicals

Since the first published studies dealing with the [2+2] photocycloaddition of enones to alkenes,[1–3] this reaction has found broad application in the synthesis of natural products as a key step in the preparation of many target molecules containing a cyclobutane ring in their skeleton.[4–7] Nevertheless, reports on the use of α,β-unsaturated lactones as substrates for [2+2] photocycloadditions are quite limited.[8–16] The synthetic utility of these reactions relies on both the regio- and stereoselectivity of the process. Studies addressed to the issue of facial diastereoselectivity in the intermolecular photocycloadditions to chiral lactones have been performed[11,13–15] and, as a result, successful stereoselective syntheses of (+)- and (–)-bourbonene[13] and (+)- and (–)-grandisol[11,14b,15c,f] have been developed.

The light induced intramolecular [2+2] cycloaddition of an enone containing an additional carbon–carbon double bond was first observed for L-carvone.[17,18] More recently, new examples have been reported,[19–22] in which the main purpose is to understand, and eventually to control, the regiochemical outcome of the process. Intramolecular photocycloadditions to α,β-unsaturated γ-lactones have also been used for the preparation of polycyclic compounds[23] and nicely applied to the asymmetric synthesis of stoechospermol.[24]

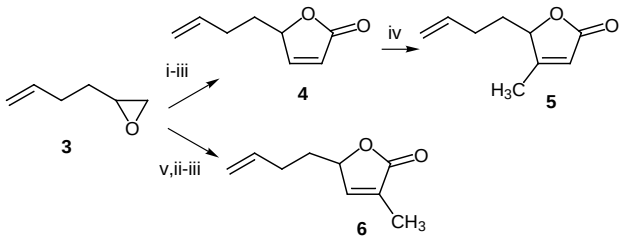
In connection with the synthesis of cyclobutanic pheromones, we were interested in the preparation of molecules with the tricyclic skeleton of **1**[25] (Scheme 1). This lactone has already been used as a key intermediate in the synthesis of (+)-grandisol[26] and several pinane[27] and bergamotane[28] derivatives. We envisaged that the α,β-butenolide **2** with an additional terminal double bond tethered to the γ-position through a two-carbon chain could be a suitable precursor for **1**, provided that the intramolecular [2+2] cycloaddition took place with the appropriate regioselectivity.



Scheme 1

The [2+2] photocycloaddition of enones is a triplet process and the regioselectivity is recognized to be originated in the diradical-forming step.[29] When cyclization is faster than reversion of the diradical to the ground-state reactants, the initial bond formation determines the regiochemistry of the products. For intramolecular processes, on the basis of experimental results, it seems to be a preference for the initial formation of a five-membered ring (rule of five),[21,30,31] although the regioselectivity may be strongly affected by electronic as well as steric factors.

To evaluate the influence of the substituents at the α and β positions on the regioselectivity of the intramolecular [2+2] cycloaddition of butenolides analogous to **2**, we decided to synthesize compounds **4**–**6** (Scheme 2) and investigate their photochemical isomerization.



Scheme 2 *Reagents and conditions*: i) $PhSeCH_2CO_2H$, LDA (2 equiv), THF, 0 ºC to r. t.; ii) AcOH, reflux; iii) H_2O_2, AcOH, THF, < 0 ºC, **4**: 95% overall; iv) CH_2N_2, Et_2O–THF, –5 ºC to r. t.; then, dioxane, reflux, **5**: 69% overall; v) $PhSeCH(Me)CO_2H$, LDA (2 equiv), THF, 0 ºC to r. t., **6**: 57% overall

Butenolides **4** and **6** were prepared through a three step sequence of reactions:[32] condensation of 1,2-epoxyhex-5-ene (**3**) with the dianion of phenylselenoacetic or 2-phe-

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able 1 Photoisomerization of Butenolides **4**–**6**

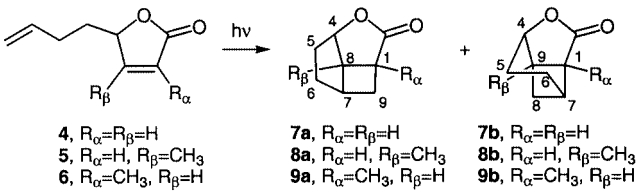
un	Substrate	λ (nm)	Filter	Solvent	Temp. (°C)	Time (h)	Yield (%)[a]	Product Isomers **a**:**b**
1[b]	**4**	254	Quartz	Et_2O	r. t.	3	30	3:1[c]
2[b]	**4**	300	Pyrex®	acetone	r. t.	5	40	3:1[c]
3[b]	**4**	350	Pyrex®	acetone	r. t.	10	40	3:1[c]
4[b]	**5**	300	Pyrex®	acetone	r. t.	8	50	7:1[c]
5[b]	**6**	300	Pyrex®	acetone	r. t.	5	58	1.6:1[c]
6	**4**	-[d]	Pyrex®	acetone	0	6	–	7:1[e]
7	**4**	-[d]	Pyrex®	acetone	–15	6	51	7:1[e]
8	**4**	-[d]	Pyrex®	acetone	–25	6	–	7:1[e]
9	**5**	-[d]	Pyrex®	acetone	–15	8	58	8:1[e]
0	**6**	-[d]	Pyrex®	acetone	–15	5	55	1.7:1[e]

Isolated yields after flash chromatography.
Irradiations were performed on a Rayonet® system.
Ratio of isolated products.
Irradiations were performed on a photochemical reactor with a 125 W medium pressure mercury lamp fitted in an immersion cooling jacket.
Ratio determined by GC of the reaction mixture.

nylselenopropionic acid, respectively, acid induced lactonization, and oxidation of the selenide function with consequent thermal elimination. Total yields were 95% for **4** and 57% for **6**. Introduction of a methyl group at the β-carbonyl position of **4** by treatment with diazomethane followed by pyrolysis of the corresponding pyrazoline afforded **5** in 69% overall yield.

Preliminary irradiation experiments were performed on a Rayonet® system at room temperature (Table 1). Degassed solutions of lactone **4** were irradiated at 254 nm (run 1), 300 nm (run 2) and 350 nm (run 3) until full conversion of the substrate. Purification by flash column chromatography gave in all three cases a ca 3:1 mixture of the regioisomers **7a** and **7b** (Scheme 3), although the isolated ratio of these isomers is not a reliable measure of the regioselectivity of the cycloaddition due to the high volatility of isomer **7a** (see below). We were unable to separate compounds **7a** and **7b**, but GC/MS analysis showed that both reaction products had the same molecular weight as the starting butenolide **4**. The structure of each isomer was assigned by ^1H and ^{13}C NMR analysis of enriched samples with the help of DEPT, COSY and $^1H/^{13}C$ correlation experiments. For the major isomer, it was observed that the β-carbonyl proton in the lactone ring was bonded to three different methine groups, a fact which is compatible with H-8 in **7a**, but not with H-9 in **7b**.

Since the irradiation of acetone solutions gave cleaner crude reaction products and the regioselectivity of the cycloaddition did not seem to be affected by the irradiation frequency, the next experiments with substrates **5** and **6** were performed under the conditions of run 2. Irradiation of **5** (run 4) took 8 hours to reach full conversion and, after



Scheme 3

flash column chromatography, afforded a 7:1 mixture of **8a** and **8b** in 50% yield. Again we were unable to separate this mixture, but the structures were assigned by GC/MS analysis and NMR experiments as above. Irradiation of **6** (run 5) for 5 hours allowed the isolation of a 1.6:1 mixture of **9a** and **9b** in 58% yield. The structure of each isomer was elucidated by GC/MS and NMR analyses of enriched mixtures as in the precedent cases. Tables 2 and 3 summarize the most significant ^1H and ^{13}C NMR data observed for compounds **7**–**9**.

Next, the experiments were repeated in a photochemical reactor using a 125 W medium pressure mercury lamp, fitted in an immersion Pyrex® cooling jacked, with a careful control of the internal temperature (entries 6–10). For these runs, the regioisomeric ratio was determined through GC analysis of the reaction mixture and it is therefore representative of the regioselectivity of the cycloaddition. It was observed that the regioselectivity was independent of the reaction temperature (compare entries 6, 7 and 8). An experiment parallel to run 7 with a fourfold diluted solution also gave the same regioisomeric ratio. The straight (head to head) regioisomer always predominates, but the proportion of the crossed (head to tail)

Table 2 ^{1}H and ^{13}C NMR Data of Compounds **7a**–**9a**,δ, *J* (Hz)

Product	H-1	H-4	H-8	C-1	C-4	C-7	C-8	C-9
7a	3.02 (m)	5.02 (dd, $J_{4,8}$ = 6.6, $J_{4,5}$ = 4.1)	3.30 (q, $J_{8,1} \approx J_{8,4} \approx J_{8,7}$ ≈ 7.1)	36.4	86.5	36.0	44.7	31.6
8a	≈ 2.7	4.53 (d, $J_{4,5}$ = 2.8)	–	41.3	91.6	41.5	52.7	28.2
9a	–	4.96 (ddd, $J_{4,8}$ = 7.2, $J_{4,5}$ = 4.5, 1.5)	2.98 (br t, $J_{8,4} \approx J_{8,7} \approx$ 7.2)	50.1	84.6	32.2	50.2	39.2

able 3 ^{1}H and ^{13}C NMR Data of Compounds **7b**–**9b**, δ, *J* (Hz)

roduct	H-1	H-4	H-9	C-1	C-4	C-7	C-8	C-9
b	2.96 (t, $J_{1,7} \approx J_{1,9} \approx$ 6.1)	–	3.09 (dq, *J* = 7.1, *J* ≈ 5.6)	46.2	82.3	37.3	24.5–23.1	40.9
b	2.63 (d, *J* = 7.0)	4.60 (br t, $J_{4,5} \approx$ 2.2)	–	51.4	87.9	34.0	30.0	–
b	–	4.99 (br d, *J* = 7.0)	2.70 (m)	42.1	81.3	43.1	23.4	44.2

cycloadduct increases substantially when the starting butenolide bears a methyl group at the α-carbonyl position and it diminishes slightly when the methyl group is at the β-carbonyl position.

To explain the regioselectivity of these reactions, the intermediate diradicals leading to each product have to be considered. For intermolecular [2+2] photocycloadditions of enones to monosubstituted olefins, attack at the less substituted terminus of the olefin is supposed to occur in the first place,[29] but for intramolecular processes steric constrains may have a decisive influence on the regioselectivity.[22] It has been demonstrated that simple molecular mechanics calculations may be used to analyze the geometry of diradical species and inter-radical distances (IRD) minor than 3 Å are considered appropriate for ring closing.[33] We have calculated the relative stability and geometry of the four possible intermediate diradicals, **I**–**IV**, for each irradiated substrate (Figure, Table 4). Molecular mechanics (MMFF94) was used for assigning the lowest energy conformer to each intermediate species and its equilibrium geometry was then optimized applying the semi-empirical AM1 model. The results are summarized in Table 4.

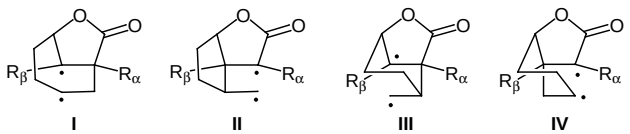


Figure Structures of intermediate diradicals **I**–**IV**

Regarding the two kind of diradicals leading to the straight adducts **7a**–**9a**, those of type **I**, coming from initial collapse of the enone α-carbon with the olefin terminal position, gave lower energies than those of type **II**, in which the initial bond is formed between the enone β-carbon and the internal olefin position, but both **I** and **II** gave suitable inter-radical distances for fast ring closing. For the intermediates leading to the crossed adducts, **III** and **IV**, those coming from initial formation of the α-carbonyl bond gave also lower energies. In these cases, moreover, the calculated inter-radical distance for the minimum energy conformation of the alternative intermediates **IV** gave too high values to favor collapse over reversion of the excited substrate to the ground state. The lower energy values and shorter inter-radical distances obtained for intermediates **I** in relation to **III** are in agreement with the regioselectivity experimentally observed in favor of the straight cycloadducts. The presence of a methyl group at the α- or β-carbonyl position has little influence on the inter-radical distance either on **I** or **III**, but the methyl group at the α-position destabilizes **I** in more extension than **III** (compare $\mathbf{I_{9a}}$ *vs* $\mathbf{I_{7a}}$ and $\mathbf{III_{9b}}$ *vs* $\mathbf{III_{7b}}$), in qualitative agreement with the lower regioselectivity observed for **6**.

Table 4 Geometrical Data for the Minimum Energy Conformation of Intermediate Diradicals **I**–**IV**[a]

Diradicals	R_α	R_β	Energy (kcal mol^{-1})[b]	IRD (Å)[c]
$\mathbf{I_{7a}/II_{7a}}$	H	H	19.3/78.9	2.7/2.8
$\mathbf{I_{8a}/II_{8a}}$	H	CH_3	20.8/84.8	2.8/2.8
$\mathbf{I_{9a}/II_{9b}}$	CH_3	H	25.0/81.3	2.7/2.9
$\mathbf{III_{7b}/IV_{7b}}$	H	H	35.1/67.9	2.9/3.8
$\mathbf{III_{8b}/IV_{8b}}$	H	CH_3	36.5/74.8	3.0/3.8
$\mathbf{III_{9b}/IV_{9b}}$	CH_3	H	37.8/70.0	2.9/3.8

[a] The calculations were performed using the PC SPARTAN pro program of Wavefunction, Inc.
[b] Energy of the most stable conformer (MMFF94).
[c] Inter-radical distance (IRD) in the most stable conformer (AM1).

In conclusion, the regioselectivity of the intramolecular [2+2] photocycloaddition of α,β-butenolides to a terminal double bond located at a suitable distance depends on the substitution pattern of the substrate. Very simple theoretical calculations performed on the diradical intermediates, considering the relative energy and inter-radical distance of the most stable conformer, are in good qualitative agreement with the experimental regioselectivity.

All solvents were purified and dried by standard techniques just before use. Diisopropylamine was freshly distilled over NaOH. Phenylselenoacetic[34] and 2-phenylselenopropionic[35] acids were prepared following previously described procedures. Photochemical reactions at r.t. were performed on a Rayonet® reactor and at lower temperatures on a standard photochemical reactor for internal irradiation with a 125 W medium pressure mercury lamp fitted in an immersion well, equipped with a Pyrex® cooling jacket. Substrate solutions were degassed by passing an argon stream through. For analytical TLC, Alugram Sil 0.25 mm thick plates Machery–Nägel were used. Chromatographic separations were carried out on silica gel 230–400 mesh activated at 80 ºC under moderated pressure (flash). GC were performed on a Hewlett-Packard 6890 chromatograph with a dimethylsilicone cross linked 12 m capillary column. GC/HRMS were recorded on a Varian MAT 311A spectrometer. Mass spectra were performed on a Hewlett-Packard 5989A spectrometer. IR spectra were obtained on a Nicolet 5ZDX spectrophotometer. ^{1}H NMR spectra were recorded on a Brucker AC250, AM400WB or 500WB instruments. Chemical shifts are given in ppm values with $CHCl_3$ as reference (set at δ = 7.24). ^{13}C NMR spectra were recorded on a Brucker AC-250, AM400WB or 500WB instruments. Theoretical calculations were performed using the PC SPARTAN pro program of Wavefunction, Inc.

5-But-3-enylfuran-2(5*H*)-one (4)

To a stirred solution of diisopropylamine (740 μL, 5.3 mmol) in THF (7 mL) under N_2 at 0 ºC was added a 1.6 M solution of BuLi in hexane (3.3 mL, 5.3 mmol) and the mixture was stirred at 0 ºC for 30 min. Then, a solution of phenylselenoacetic acid (516 mg, 2.4 mmol) in THF (10 mL) was added dropwise. A white precipitate was immediately formed. Next, a solution of epoxide **3** (225 μL, 2.0 mmol) in THF (10 mL) was added drop-wise, the cooling bath was removed and the reaction mixture was stirred at r. t. for 5 h. The mixture was acidified with glacial AcOH and the resulting solution was heated at reflux overnight. After neutralization with sat. aq $NaHCO_3$, the mixture was extracted with Et_2O (3 × 25 mL). The organic extracts were dried (Na_2SO_4) and concentrated to give an oily residue (662 mg) which purified by flash chromatography (eluent: EtOAc–hexane, 1:3) afforded a mixture of *cis*- and *trans*-5-(but-3-enyl)-3-phenylseleno-2-oxolanone (572 mg, 97%) as a pale yellow oil.

IR (film): ν = 3069, 2980, 2931, 1774, 1474, 1442, 1353, 1183, 1021 cm^{-1}.

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.55 (m, 2 H), 7.25 (m, 3 H), 5.65 (m, 1 H), 4.92 (m, 2 H), 4.32 and 4.23 (m, 1 H), 3.94 (t, *J* = 9.5 Hz) and 3.86 (dd, *J* = 6.6, 4.0 Hz) (total 1 H), 2.64 (ddd, *J* = 13.5, 9.5, 6.4 Hz) and 2.30–1.4 (complex absorption) (total 6 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 175.6, 136.8, 136.7, 135.8, 135.7, 135.6, 135.4, 129.4, 129.3, 129.1, 128.8, 115.7, 115.6, 78.7, 78.4, 77.5, 77.0, 76.5, 37.4, 37.0, 36.7, 36.6, 35.8, 34.6, 34.3, 29.3, 29.2.

Anal. Calcd for $C_{14}H_{16}O_2Se$: C, 56.96; H, 5.46; found C, 56.91; H, 5.56.

To a stirred, cold solution of 5-(but-3-enyl)-3-phenylseleno-2-oxolanone (276 mg, 0.93 mmol) and AcOH (2 drops) in THF (3 mL) was added drop-wise 30% H_2O_2 (0.80 mL, 7.0 mmol), keeping the temperature below 0 ºC. The mixture was stirred at 0 ºC for 45 min, then neutralized with sat. aq $NaHCO_3$ and extracted with Et_2O (3 × 10 mL). The organic extracts were dried (Na_2SO_4) and the solvent evaporated under vacuum. The oily residue was distilled on a Kugelrohr (70–75 ºC, oven temp./0.06 Torr) to afford **4** (127 mg, 98%) as a colorless oil.

IR (film): ν = 3084, 2927, 1754, 1164, 1105 cm^{-1}.

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.45 (dd, *J* = 5.6, 1.5 Hz, 1 H), 6.08 (dd, *J* = 5.6, 2.0 Hz, 1 H), 5.77 (ddt, J_{trans} = 17.2 Hz, J_{cis} = 10.2 Hz, *J* = 6.6 Hz, 1 H), 5.06 (m, 3 H), 2.21 (m, 2 H), 1.82 (m, 1 H), 1.77 (m, 1 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 172.9, 156.1, 136.6, 121.5, 116.1, 82.5, 32.3, 29.1.

MS: *m/z* (%) = 139 (M^+ + 1, 1), 138 (M^+, 2), 110 (5), 84 (100), 55 (74).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.30; found C, 69.38; H, 7.40.

5-But-3-enyl-4-methylfuran-2(5*H*)-one (5)

An ethereal solution of diazomethane (ca 3.80 mmol) prepared from Diazald® (1.09 g, 5.09 mmol) was slowly distilled over to a stirred solution of **4** (245 mg, 1.8 mmol) in THF (4 mL) at –5 ºC. The mixture was kept in the dark, at r. t. for 24 h, monitoring the reaction by TLC (eluent: EtOAc–hexane, 1:1). Evaporation of the solvent gave a white solid identified as 4-(but-3-enyl)-3a,4,6,6a-tetrahydro-3*H*-furo[3,4-*c*]pyrazol-6-one (323 mg, ~100%) which was not further purified:

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.75 (ddt, J_{trans} = 17.0 Hz, J_{cis} = 10.1 Hz, *J* = 6.6 Hz, 1 H), 5.50 (td, *J* = 2.5, 2.2 Hz, 1 H), 4.98 (m, 2 H), 4.82 (dt, J_{gem} = 18.6 Hz, *J* = 2.5 Hz, 1 H), 4.67 (ddd, J_{gem} = 18.6 Hz, *J* = 8.2 Hz, *J* = 1.9 Hz, 1 H), 3.92 (m, 1 H), 2.62 (m, 1 H), 2.16 (m, 2 H), 1.78 (m, 1 H), 1.71 (m, 1 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 168.0, 136.2, 116.3, 94.3, 85.2, 85.1, 37.9, 35.6, 29.1.

This solid was dissolved in freshly distilled 1,4-dioxane (25 mL) and heated at reflux for 48 h, following the reaction progress by TLC (eluent: EtOAc–hexane, 1:1). Evaporation of the solvent under vacuum gave a crude product which was purified by flash chromatography (eluent: EtOAc–hexane, 1:2) affording **5** (185 mg, 69%) as a colorless oil.

IR (film): ν = 3079, 2984, 2924, 1751, 1643, 1439, 1296, 1170 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.78 (m, 2 H), 5.03 (m, 2 H), 4.82 (d, *J* = 7.9 Hz, 1 H), 2.19 (m, 2 H), 2.03 (s, 3 H), 1.97 (m, 1 H), 1.56 (m, 1 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 173.1, 168.4, 136.7, 117.0, 116.1, 83.8, 31.4, 28.7, 13.8.

HRMS: *m/z* calcd for $C_9H_{12}O_2$ (M^+) 152.0837, found 152.0842.

MS: *m/z* (%) = 153 (M^+ + 1, 1), 152 (M^+, 2), 110 (12), 98 (100), 69 (40), 41 (79).

5-But-3-enyl-3-methylfuran-2(5*H*)-one (6)

To a stirred solution of diisopropylamine (4.2 mL, 30.0 mmol) in THF (40 mL) under N_2 at 0 ºC was added a 1.6 M solution of BuLi in hexane (18.7 mL, 30.0 mmol) and the mixture was stirred for 30 min. Then, a solution of 2-phenylselenopropionic acid (3.44 g, 15.0 mmol) in THF (10 mL) was added drop-wise and the mixture was stirred at 0 ºC for 15 min and at 40 ºC for 30 min. Then the reaction mixture was cooled again to 0 ºC, a solution of epoxide **3** (1.6 mL, 14.2 mmol) in THF (40 mL) was added, the cooling bath removed and the mixture stirred at r. t. for 4 h. The mixture was acidified with glacial AcOH and the resulting solution was heated at reflux over-

night. After neutralization with sat. aq $NaHCO_3$, the mixture was extracted with Et_2O (3 × 200 mL). The organic extracts were dried (Na_2SO_4) and concentrated to give an oily residue which purified by flash chromatography (eluent: EtOAc–hexane, 1:3) afforded a mixture of the two diastereoisomers of 5-(but-3-enyl)-3-phenylseleno-3-methyl-2-oxolanone (3.61 g, 80%) as a pale yellow oil:

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64 (m, 2 H), 7.40 (m, 1 H), 7.32 (m, 2 H), 5.74 (m, 1 H), 5.00 (m, 2 H), 4.40 (m, 1 H), 2.41 (m, 1 H), 2.20–2.05 (complex absorption) and 1.91 (dd, *J* = 14.0, 10.4 Hz) (total 3 H), 1.78 (m, 1 H), 1.68–1.50 (complex absorption, 4 H).

To a stirred, cool solution of this oil and AcOH (a few drops) in THF (25 mL) was added drop-wise 30% H_2O_2 (9.0 mL, 79 mmol), keeping the temperature below 0 ºC. The mixture was stirred at 0 ºC for 45 min, then neutralized with sat. aq $NaHCO_3$ and extracted with Et_2O (3 × 30 mL). The organic extracts were dried (Na_2SO_4) and the solvent evaporated under vacuum. The oily residue was purified by flash chromatography (eluent: EtOAc–hexane, 1:4) to afford **6** (1.23 g, 71%) as a colorless oil; bp 50–55 ºC (oven temp.)/0.7 Torr.

IR (film): ν = 3083, 2926, 1755, 1647, 1449, 1100, 1058 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.01 (m, 1 H), 5.76 (ddt, J_{trans} = 17.0 Hz, J_{cis} = 10.1 Hz, *J* = 6.6 Hz, 1 H), 5.03 (dm, J_{trans} = 17.0 Hz, 1 H), 4.98 (dm, J_{cis} = 10.1 Hz, 1 H), 4.87 (m, 1 H), 2.18 (m, 2 H), 1.87 (s, 3 H), 1.78 (m, 1 H), 1.67 (m, 1 H).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 174.2, 148.6, 136.9, 130.1, 116.0, 80.4, 32.7, 29.3, 10.6.

HRMS: *m/z* calcd for $C_9H_{12}O_2$ (M^+) 152.0837, found 152.0839.

MS: *m/z* (%) = 152 (M^+, 2), 124 (10), 110 (34), 98 (76), 97 (54), 69 (46), 55 (92), 41 (100).

Irradiation of 5-But-3-enylfuran-2(5*H*)-one (4) at Room Temperature; General Procedure

A solution of **4** (100 mg, 0.72 mmol) in acetone (10 mL) placed in a Pyrex® vessel was irradiated on a Rayonet® reactor suited with 300 nm lamps for 5 h. The progress of the reaction was followed by GC. The solvent was evaporated and the oily residue was purified by flash chromatography (eluent: CH_2Cl_2–hexane, 3:2), affording a 3:1 mixture of 3-oxatricyclo[5.1.1.0^{4,8}]nonan-2-one (**7a**) and of 3-oxatricyclo[5.2.0.0^{4,9}]nonan-2-one (**7b**) (40 mg, 0.29 mmol, 40%); bp 70–75 ºC (oven temp.)/0.1 Torr.

7a and **7b**

IR (film): ν = 2966, 2936, 2870, 1769, 1356, 1170, 1050, 1003 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): Signals assigned to **7a**; δ = 5.02 (dd, $J_{4,8}$ = 6.6 Hz, $J_{4,5}$ = 4.1 Hz, 1 H, H-4), 3.30 (q, $J_{8,1} \approx J_{8,4} \approx J_{8,7} \approx$ 7.1 Hz, 1 H, H-8), 3.02 (m, 1 H, H-1), 2.85–2.74 (complex absorption, 2 H, H-7 and H-9), 2.31 (m, 1 H, H-5/H-6), 2.26 (m, 1 H, H-5/H-6), 1.76–1.63 (complex absorption, 3 H, H-5, H-6 and H-9). Signals assigned to **7b**; δ = 3.09 (dq, *J* = 7.1 Hz, *J* ≈ 5.6 Hz, 1 H, H-9), 2.96 (t, *J* ≈ 6.1 Hz, 1 H, H-1).

^{13}C NMR ($CDCl_3$, 125 MHz): Signals assigned to **7a**; δ = 181.0 (C-2), 86.5 (C-4), 44.7 (C-8), 36.6 (C-5/C-6), 36.4 (C-1), 36.0 (C-7), 31.7 (C-5/C-6), 31.6 (C-9). Signals assigned to **7b**; δ = 178.0 (C-2), 82.3 (C-4), 46.2 (C-1), 40.9 (C-9), 37.3 (C-7), 24.5/23.9/23.1 (C-5/C-6/C-8).

GC (T_1 = 80 ºC, t_1 = 1 min, T_2 = 240 ºC, rate = 10 ºC/min): **7a** 8.17 min, **7b** 8.29 min.

HRMS: *m/z* calcd for $C_8H_{10}O_2$ (M^+) 138.0681, found **7a** 138.0701, **7b** 138.0701.

MS: *m/z* (%) **7a** = 139 (M^+ + 1, 1), 138 (M^+, 6), 79 (50), 66 (100), 55 (28), 39 (50); **7b** = 138 (M^+, 4), 110 (20), 84 (96), 83 (44), 79 (60), 66 (60), 55 (42), 39 (100).

Irradiation of 5-But-3-enyl-4-methylfuran-2(5*H*)-one (5) at Room Temperature

Irradiation of **5** (105 mg, 0.69 mmol) for 8 h following the general procedure gave a 7:1 mixture of 8-methyl-3-oxatricyclo[5.1.1.0^{4,8}]nonan-2-one (**8a**) and of 9-methyl-3-oxatricyclo[5.2.0.0^{4,9}]nonan-2-one (**8b**) (52 mg, 50%); bp 90–95 ºC (oven temp.)/0.1 Torr.

8a and **8b**

IR (film): ν = 2960, 2930, 2870, 1769, 1451, 1284, 1164, 1044 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): Signals assigned to **8a**; δ = 4.53 (d, $J_{4,5}$ = 2.8 Hz, 1 H, H_4), 2.76–2.62 (complex absorption, 2 H, H-1 and H-9), 2.29 (m, 1 H, H-7), 2.20 (m, 1 H, H-5), 2.14 (m, 1 H, H-6), 1.81–1.64 (complex absorption, 3 H, H-5, H-6 and H-9), 1.28 (s, 3 H, CH_3). Signals assigned to **8b**; δ = 4.60 (br t, $J_{4,5} \approx$ 2.2 Hz, 1 H, H-4), 2.63 (d, *J* = 7.0 Hz, 1 H, H-1), 1.19 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 125 MHz): Signals assigned to **8a**; δ = 180.8 (C-2), 91.6 (C-4), 52.7 (C-8), 41.5 (C-7), 41.3 (C-1), 35.0 (C-6), 32.5 (C-5), 28.2 (C-9), 20.5 (CH_3). Signals assigned to **8b**; δ = 87.9 (C-4), 51.4 (C-1), 34.0 (C-7), 30.0 (C-8), 24.6 (C-5), 22.4 (C-6), 22.1 (CH_3).

GC (T_1 = 60 ºC, t_1 = 2 min, T_2 = 240 ºC, rate = 10 ºC/min): **8a** 10.85 min, **8b** 10.93 min.

HRMS: *m/z* calcd for $C_9H_{12}O_2$ (M^+) 152.0837, found **8a** 152.0850, **8b** 152.0850.

MS: *m/z* (%) **8a** = 152 (M^+, 6), 124 (5), 110 (11), 98 (100); **8b** = 152 (M^+, 10), 124 (12), 109 (13), 98 (100), 80 (61), 39 (45).

Irradiation of 5-But-3-enyl-3-methylfuran-2(5*H*)-one (6) at Room Temperature

Irradiation of **6** (105 mg, 0.69 mmol) for 5 h following the general procedure gave a 1.6:1 mixture of 1-methyl-3-oxatricyclo[5.1.1.0^{4,8}]nonan-2-one (**9a**) and of 1-methyl-3-oxatricyclo[5.2.0.0^{4,9}]nonan-2-one (**9b**) (61 mg, 58%); bp 90–95 ºC (oven temp.)/0.2 Torr.

9a and **9b**

IR (film): ν = 2962, 2932, 2865, 1770, 1455, 1352, 1231, 1128, 1086 cm^{-1}.

^{1}H NMR ($CDCl_3$, 500 MHz): Signals assigned to **9a**; δ = 4.96 (ddd, $J_{4,8}$ = 7.2 Hz, $J_{4,5}$ = 4.5 Hz, $J_{4,5}$ = 1.5 Hz, 1 H, H-4), 2.98 (br t, $J_{8,4} \approx J_{8,7} \approx$ 7.2 Hz, 1 H, H-8), 2.71 (m, 1 H, H-7), 2.34 (dd, J_{gem} = 12.6 Hz, $J_{9,7}$ = 8.8 Hz, 1 H, H-9), 2.25 (m, 1 H, H-5), 2.12 (m, 1 H, H-6), 1.92 (dd, J_{gem} = 12.6 Hz, $J_{9,7}$ = 3.5 Hz, 1 H, H-9), 1.73–1.58 (complex absorption, 2 H, H-5 and H-6), 1.34 (s, 3 H, CH_3). Signals assigned to **9b**; δ = 4.99 (br d, *J* ≈ 7.0 Hz, 1 H, H-4), 2.70 (m, 1 H, H-9), 2.35 (m, 1 H, H-7), 2.23 (m, 1 H, H-8), 2.00–1.90 (complex absorption, 4 H, 2 H-5 and 2 H-6), 1.34 (s, 3 H, CH_3).

^{13}C NMR ($CDCl_3$, 125 MHz): Signals assigned to **9a**; δ = 183.0 (C-2), 84.6 (C-4), 50.2 (C-8), 50.1 (C-1), 39.2 (C-9), 36.5 (C-5), 32.2 (C-7), 31.5 (C-6), 21.5 (CH_3). Signals assigned to **9b**; δ = 180.1 (C-2), 81.3 (C-4), 44.2 (C-9), 43.1 (C-7), 42.1 (C-1), 23.9 (C-5), 23.6 (C-6), 23.4 (C-8), 16.7 (CH_3).

GC (T_1 = 80 ºC, t_1 = 1 min, T_2 = 240 ºC, rate = 10 ºC/min): **9a** 7.72 min, **9b** 8.18 min.

HRMS: *m/z* calcd for $C_9H_{12}O_2$ (M^+) 152.0837, found **9a** 152.0857, **9b** 152.0854.

MS: *m/z* (%) **9a** = 152 (M^+, 3), 93 (31), 80 (100), 67 (32), 41 (47); **9b** = 152 (M^+, 10), 124 (23), 110 (41), 98 (100), 96 (85), 55 (78), 41 (74), 39 (75).

Irradiation of 5-But-3-enylfuran-2(5*H*)-one (4) at Low Temperature; General Procedure

A solution of **4** (89 mg, 0.65 mmol) in acetone (80 mL) at –15 ºC was irradiated for 6 h. MeOH was used for refrigeration of the immersion well jacket and an external bath at –50 ºC was also necessary to keep the temperature of the reaction mixture at –15 ºC. The reaction progress was monitored by GC. After total conversion of **4**, the ratio **7a**/**7b** was 7:1. The solvent was evaporated and the oily residue was purified by flash chromatography (eluent: CH_2Cl_2–hexane, 1:1), affording a 6:1 mixture of **7a** and **7b** (45 mg, 51%). Repeated flash chromatography allowed the isolation of a fraction (18 mg) containing a 14:1 mixture (^{1}H NMR analysis) of **7a** and **7b**.

Irradiation of 5-But-3-enyl-4-methylfuran-2(5*H*)-one (5) at Low Temperature

Irradiation of **5** (80 mg, 0.53 mmol) at –15 ºC following the general procedure showed total conversion of the substrate after 8 h, giving a 8:1 mixture (GC) of **8a** and **8b**. Purification by flash chromatography (eluent: CH_2Cl_2–hexane, 1:1) afforded a 10:1 mixture of **8a** and **8b** (46 mg, 58%). A second flash chromatography allowed isolation of **8a** (14 mg) of more than 98% purity (^{1}H NMR analysis).

Irradiation of 5-But-3-enyl-3-methylfuran-2(5*H*)-one (6) at Low Temperature

Irradiation of **6** (74 mg, 0.49 mmol) at –15 ºC following the general procedure showed total conversion of the substrate after 5 h, giving a 1.7:1 mixture (GC) of **9a** and **9b**. Purification by flash chromatography (eluent: CH_2Cl_2–hexane, 1:1) afforded a 1.5:1 mixture of **9a** and **9b** (41 mg, 55%).

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