Pergamon

Tetrahedron 58 (2002) 2331–2338

TETRAHEDRON

Mechanistic studies of the photochemical rearrangement of 1-oxolongipin-2-ene derivatives

Myriam Meléndez-Rodríguez,[a] Carlos M. Cerda-García-Rojas,[a] César A. N. Catalán[b] and Pedro Joseph-Nathan[a,*]

[a]*Departamento de Química del Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Apartado 14-740, México D.F., 07000 Mexico*

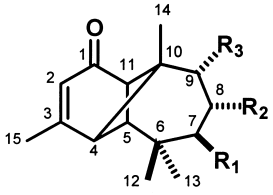
[b]*Instituto de Química Orgánica, Facultad de Bioquímica, Química y Farmacia, Universidad Nacional de Tucumán, Ayacucho 491, S.M. de Tucumán, 4000 Argentina*

Received 3 December 2001; accepted 31 January 2002

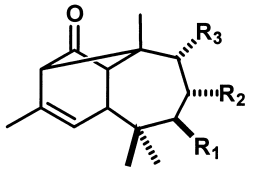
Abstract—Ultraviolet irradiation of (4*R*,5*S*,7*S*,8*R*,9*S*,10*R*,11*R*)-7,8,9-triacetyloxy-1-oxolongipin-2-ene (**2**) afforded the vulgarone A **7** and the pingilonene **8** derivatives as the major products, which were formed by a [1,3]-shift, together with the minor secondary photoproducts **9** and **10**. The phototransformation mechanism is discussed in terms of individual ultraviolet irradiation of **7** and **8** in combination with the monitoring reaction progress of **2** by ^{1}H NMR measurements. The stereostructures of the new carbocyclic skeleta were geometry optimized using density functional calculations.

1. Introduction

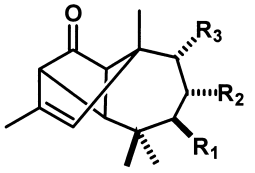
Highly functionalized longipinene derivatives of types **1** and **2** are relevant secondary metabolites in many species of the *Stevia* genus.[1] The chemical reactivity of this class of substances, whose absolute configuration is known,[2] has been widely studied, in particular, their versatility towards chemically induced molecular rearrangements.[3–7] In contrast, its photoreactivity has been scarcely explored even though this study could provide new approaches to unusual and highly functionalized tricyclic sesquiterpenes. In a previous work on the photochemical reactivity of the longipinene ring system, the conversion of vulgarone B (**3**) into vulgarone A (**4**) and other unspecified products has been described.[8,9] Also, in a preliminary communication, we reported the photochemical transformation of longipinene derivatives **1** and **2** into the new vulgarone A derivatives **5** and **7** and the new pingilonene derivatives **6** and **8**.[10] Diacetylated photopoducts **5** and **6** were separated with some difficulties, while triacetylated products **7** and **8** were easily purified. Also, the NMR spectra of **2**, **7** and **8** exhibited a simpler profile than those of less functionalized longipinenes, simplifying their structure elucidation and NMR assignments. Therefore, compound **2** was selected to carry out a detailed study on the photochemical reactivity of the longipinene structure, including a plausible reaction mechanism based on reaction progress ^{1}H NMR measure-



1 : $R_1 = R_3 = OAc$; $R_2 = H$
2 : $R_1 = R_2 = R_3 = OAc$
3 : $R_1 = R_2 = R_3 = H$



4 : $R_1 = R_2 = R_3 = H$
5 : $R_1 = R_3 = OAc$; $R_2 = H$
7 : $R_1 = R_2 = R_3 = OAc$

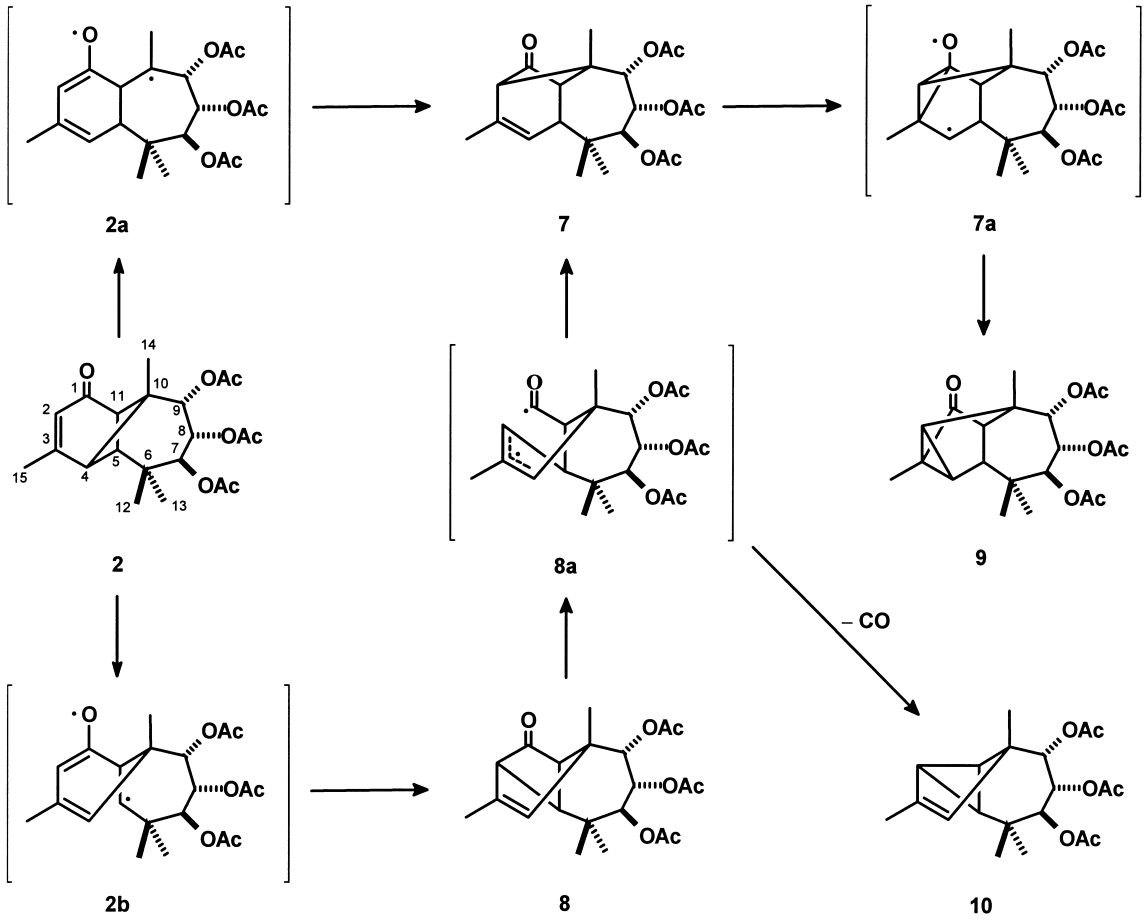


6 : $R_1 = R_3 = OAc$; $R_2 = H$
8 : $R_1 = R_2 = R_3 = OAc$

Keywords: photochemistry; mechanisms; molecular modeling; density functional calculations; terpenes; longipinene.

* Corresponding author. Tel.: +5255-5747-7112; fax: +5255-5747-7137; e-mail: pjoseph@nathan.chem.cinvestav.mx

0040–4020/02/$ - see front matter
PII: S0040-4020(02)00121-7



Scheme 1. Photochemical reactivity of 7,8,9-triacetyloxy-1-oxolongipin-2-ene (**2**).

ments and the individual ultraviolet irradiation of the major photoproducts **7** and **8**.

2. Results and discussion

UV irradiation of triacetate **2**[11] in cyclohexane for 5 min using a low pressure mercury arc lamp at room temperature afforded two rearranged β,γ-unsaturated ketones **7** (56%) and **8** (15%) along with two novel rearranged products **9** (1%) and **10** (3%) (Scheme 1). Starting compound was recovered in 3% and the remnant was constituted by unspecified tarry materials.

2.1. Mechanistic studies

In order to determine the role played by the minor products **9** and **10** and to study the formation mechanism of **7** and **8**, we performed: (i) the individual ultraviolet irradiation of the major photoproducts **7** and **8**, and (ii) the photochemical transformation of **2** monitored by ^{1}H NMR measurements.

The photoreactivity of products **7** and **8** was studied by direct irradiation under the same reaction conditions as those used for **2**. The ^{1}H NMR analysis of the crude material obtained from irradiation of **7** for 30 min gave the tetracyclic compound **9** as the only product in 30%, together with unchanged starting material (70%). On the other hand, the ^{1}H NMR spectrum of the crude material obtained after irradiation of compound **8** for 30 min revealed a mixture of **7**, **9** and **10** in 17, 9 and 37%, respectively, and starting material (**8**) in 37%. It is noteworthy to mention that **7** is obtained from **8** in smaller amounts (17%) than directly from **2** (51%) under the same reaction conditions (Table 1, at 5 min). These findings indicated that the main β,γ-unsaturated ketones **7** and **8**, formed from **2** by [1,3]-shifts of the C(4)–C(10) or C(4)–C(5) bonds, respectively, are primary photoproducts, while the minor compounds **9** and **10** derived from **7** and **8**, respectively, are secondary photoproducts. This behavior was clearly observed when the phototransformation of **2** was followed by ^{1}H NMR analysis, as shown in Table 1. The measurements were performed by integration of the ^{1}H NMR methyl signals

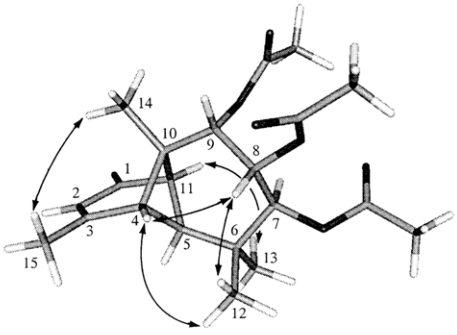
Table 1. Product composition (%) obtained by irradiation of **2** in cyclohexane

Compound	Irradiation time (min)				
	5	10	20	30	60
7	72	68	63	51	37
8	24	22	20	18	17
9	–[a]	–[a]	5	6	14
10	4	10	12	25	32

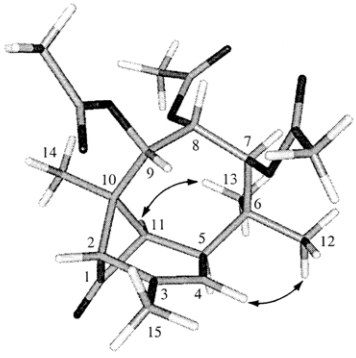
[a] Not observed.

of the photoproducts in the crude reaction mixtures obtained after irradiation of solutions of **2** in cyclohexane (0.077 mmol) during several time intervals. The results obtained for **2** demonstrate the fast production of **7** and **8** and the subsequent appearance of **9** and **10** with the corresponding disappearance of **7** and **8**. Considering the photoreactivity described in the literature for β,γ-unsaturated carbonyl systems,[12] compound **7** might be converted into **9** by an oxadi-π-methane rearrangement, which could result in a formal [1,2]-acyl shift involving formation of the C(1)–C(3) bond with subsequent cleavage of the C(1)–C(2) bond and reclosure to a cyclopropyl ring by the C(2)–C(4) bonding. Rearrangement of **8** to **7** or **10** could proceed by an initial ketonic α cleavage giving the intermediate **8a**, followed by a [1,3]-acyl shift to yield **7** or decarbonylation to afford **10** (Scheme 1).

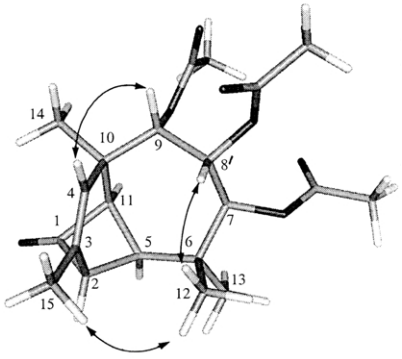
It is described that direct irradiation of β,γ-unsaturated ketones generally leads to [1,3]-acyl shifts whereas triplet sensitization may result in an oxadi-π-methane rearrangement.[12] A few exceptions have been reported in which oxadi-π-mehane reactions were observed upon direct irradiation.[13–16] In such cases, the explanation for the differences in photoreactivity is related to the degree of overlapping between the double bond and the carbonyl function, in which an effective overlap favored the α-cleavage. It has also been proposed that the stability of the allyl radical species formed by α-fission as well as the ground-state geometry may play an important role in the α-cleavage process.[12,15,16] In our case, we observed that under direct irradiation, compound **8** underwent the [1,3]-acyl shift, while **7** showed the oxadi-π-methane rearrangement. This last reaction corresponds to an additional



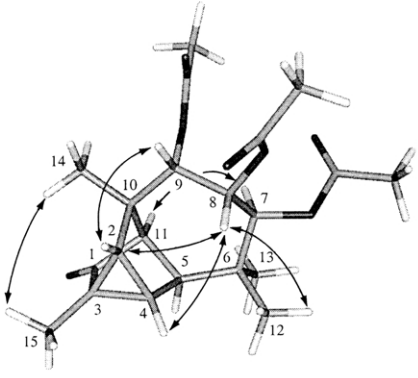
2 (E_{DFT} = −1344.19344 hartrees)



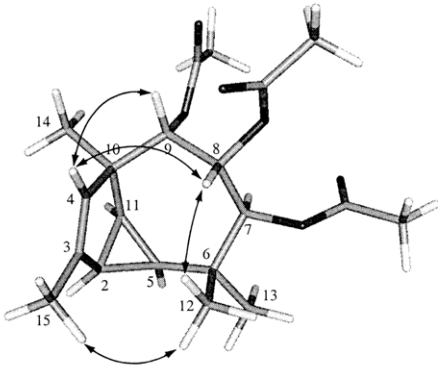
7 (E_{DFT} = −1344.18012 hartrees)



8 (E_{DFT} = −1344.17843 hartrees)



9 (E_{DFT} = −1344.20236 hartrees)



10 (E_{DFT} = −1230.80508 hartrees)

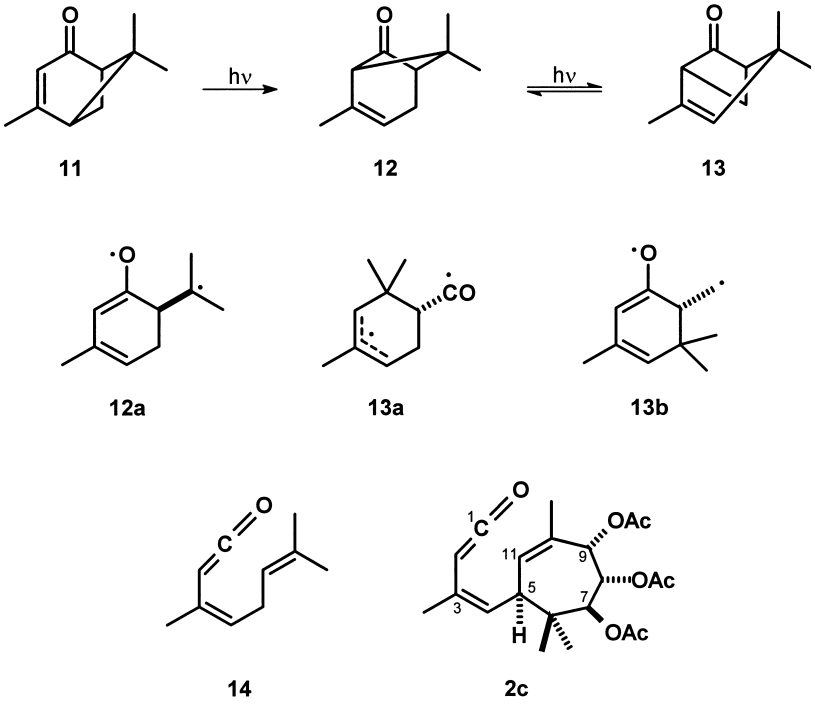
Figure 1. Minimum energy conformation using density functional theory, and relevant NOESY correlations for **2** and photoproducts **7**–**10**.

example of uncommon photochemical reactivity displayed by β,γ-unsaturated ketones. The minimized structures of **7** and **8** (Fig. 1) show an equivalent geometry for the β,γ-unsaturated moiety in both compounds, which is reflected in their similar UV spectra: **7** λ_{max} (EtOH) 283 nm (ϵ 195) and **8** λ_{max} (EtOH) 286 nm (ϵ 162). On the other hand, the allyl radical intermediate which could result from the C(1)–C(2) bond cleavage is the same (**8a**) for both substances. Therefore, the strong difference in the photochemical behavior of **7** vs. **8** is neither related to the degree of overlapping between the double bond and the carbonyl function, nor to the stability of the allyl radical species formed during the α-fission. In contrast, the ground-state geometry of the complete molecules (Fig. 1), including the influence of the chiral centers at C-5, C-7, C-8, C-9, C-10 over the β,γ-unsaturated moiety may be responsible for the reactivity difference observed in **7** and **8**.

A photoinduced [1,3]-shift has been reported to occur for the transformation of verbenone (**11**) into chrysanthenone (**12**)[17–20] (Scheme 2). In one of these papers,[18] it was stated that chrysanthenone (**12**) was obtained as a primary product from **11** via intermediate **12a**, while 2,4,4-trimethylbicyclo[3.1.1]hept-2-en-6-one (**13**) was formed as a secondary photoproduct from **12** by a reversible [1,3]-acyl shift isomerization throughout intermediate **13a**. However, the possibility that some of **13** was produced directly from **11** via a less stable primary radical (**13b**) was not completely ruled out. Also, partial loss of the optical activity observed during formation of **12** was explained by the participation of the optically inactive species **14** as a reaction intermediate arising from **12a**[18] (Scheme 2). Considering these arguments, we can postulate that the transformation of **2** into **7** and **8** could proceed through intermediates **2a** and **2b**, respectively. Species **2a** contains a tertiary radical, which is more stable than the secondary radical in species **2b**. This fact could explain the yield differences for **7** (56%) and **8** (15%) upon direct irradiation of **2**. When closely comparing the photochemical behavior of **2** and **11**, we found differences which can again be attributed to the presence of the additional cycloheptane ring and its chiral centers. For example, the reversible photoisomerization[18] between **12** and **13** does not take place in the case of longipinenes **7** and **8**. Also, compound **8** is a primary photoproduct, while the analogous compound **13** is a secondary one. On the other hand, if a ketene intermediate such as **2c** is formed during the reaction pathway, its ring reclosure is governed by the chiral centers of the seven-membered ring, mainly that at C-5.

2.2. Structure elucidation using molecular modeling and NMR spectroscopy

The structures of **7**–**10** were mainly determined by 1D and 2D NMR spectroscopy and HRMS. Also, since photoproducts **7**–**10** contained novel carbocyclic skeleta, it was desirable to visualize their tridimensional perspectives by using molecular modeling calculations and to correlate the stereostructure of each compound with the corresponding spectral properties. Thus, the configuration of all stereogenic centers and the conformation in solution of **7**–**10** were determined on the basis of the calculated and observed ^1H–^1H coupling constants and the information provided by the NOESY spectra, in combination with the molecular models represented in Fig. 1 and taking into account the absolute configuration of **2**.[2,11] The minimum energy conformation of **2** and its photoproducts **7**–**10** (Fig. 1) were obtained by molecular mechanics calculations (MMX)[21] followed by geometry optimization using density functional theory calculations at the pBP/DN** level.[22] In Fig. 1, the minimum energy structure for **2** shows a twist-chair seven-membered ring conformation in which the substituents at C-7 and C-8 are *pseudo*-equatorial, while



Scheme 2. Photochemical reactivity of verbenone (**11**).[17–20]

Table 2. Selected dihedral angles (ϕ_{DFT} in degrees), calculated coupling constants (J_{calc} in Hz) and observed coupling constants (J_{obs} in Hz) for **2** and photoproducts **7**–**10**

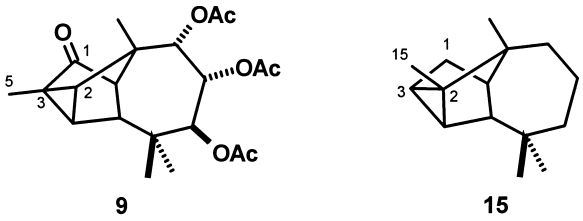
Compound	H(7)–C(7)–C(8)–H(8)			H(8)–C(8)–C(9)–H(9)		
	ϕ_{DFT} [a]	J_{calc} [b]	J_{obs} [c]	ϕ_{DFT} [a]	J_{calc} [b]	J_{obs} [c]
2	164.8	10.0	11.0	61.7	2.2	2.9
7	−49.5	5.3	5.8	−76.7	1.0	1.1
8	160.8	9.9	10.4	65.9	1.8	2.3
9	157.3	9.7	10.2	65.8	1.8	2.0
10	169.6	10.1	10.5	64.8	1.9	2.2

[a] From density functional theory at the pBP/DN** level.[22]
[b] From calculated dihedral angles.[23,24]
[c] Measured at 300 MHz in $CDCl_3$.

that at C-9 remains *pseudo*-axial. The NOESY data and the calculated[23,24] and observed coupling constant values $J_{7,8}$ and $J_{8,9}$ (Fig. 1 and Table 2) indicated that compounds **8**–**10** preserve the seven-membered ring conformation originally present in the longipinene system,[2] while compound **7** exists in a conformation where the substituents at C-7 and C-8 are *pseudo*-axial and the substituent at C-9 is *pseudo*-equatorial. The W-type long-range coupling[25] between H-5 and H-7 (1.4 Hz) observed in **7** supported the half-chair conformation for the cycloheptane ring.

Photoproducts **7** and **8** showed IR cyclobutanone carbonyl absorptions around 1775 cm^{-1} and had identical molecular formula $C_{21}H_{28}O_7$ as established by HRMS in combination with ^1H and ^{13}C NMR data. Their UV and EIMS data were also markedly similar indicating the presence of a β,γ-unsaturated cyclobutanone. The ^1H NMR spectra of **7** and **8** showed signals due to the same kind of protons: one vinylic proton, three protons geminal to an acetyloxy group, three acetate methyl groups, three methyne protons, and one vinylic and three tertiary methyl groups. Interpretation of COSY, HETCOR, FLOCK[26] and NOESY spectra indicated that **7** corresponded to the 7,8,9-triacetyloxy derivative of vulgarone A (**4**),[9,10,27] while compound **8** possesses the hydrocarbon skeleton which we named pingilonene.[10] The COSY spectrum of vulgarone A derivative **7** evidenced the W-type coupling between H-2 at 2.92 and H-11 at 3.28, characteristic of rigid four-membered rings.[28] NOESY interactions between H-2 and Me-14 and between H-11 and Me-14 allowed a clear assignment for these nuclei. Also, the signal for H-11 showed a NOESY interaction with the signal for Me-13, while the signal for the vinylic proton H-4 displayed a NOESY interaction with that for Me-12 (Fig. 1). The FLOCK spectrum was very useful to assign the quaternary carbons C-6 and C-10, since the signal at δ 40.1, assigned to C-6, showed correlations with the proton signals for the *gem*-dimethyl group, while the signal at δ 35.4, assigned to C-10, showed a correlation with the proton signal for Me-14. The ^1H NMR of pingilonene derivative **8** displayed signals for the three protons attached to the four-membered ring at δ 3.27 (H-11), 3.14 (H-2) and 2.36 (H-5), with the corresponding long-range coupling between H-2 and H-11 of J=6.8 Hz.[28] The vinylic proton signal at δ 5.31 showed a strong NOESY interaction with the signal at δ 5.16, assigned to H-9, while the signal for Me-12 (δ 1.17) displayed intense NOESY interactions with the signals for H-8 (δ 5.20) and Me-15 (δ 1.86), in agreement with the molecular model of **8** represented in Fig. 1.

Compound **9** had the molecular formula $C_{21}H_{28}O_7$ as deduced from HRMS. Its structure was established by 1D and 2D NMR data in $CDCl_3$ and in C_6D_6. The IR absorption band at 1744 cm^{-1} was consistent with a cyclopentanone moiety. The ^1H NMR spectrum displayed signals for three protons geminal to acetyloxy groups, three acetate methyl groups, four methyne protons and four tertiary methyl groups. The C-2/H-2 (176 Hz) and C-4/H-4 (177 Hz) coupling constants obtained by ^1H gated decoupling confirmed the presence of a three-membered ring.[29] The relevant NOESY interactions for this structure are marked in Fig. 1. The ^{13}C NMR signal for one tertiary methyl group (Me-15) at δ=8.5 indicated that this group is attached to the cyclopropane unit. Its position at C-3 was established by the C-1/Me-15 FLOCK correlation. The hydrocarbon skeleton of **9** resembles that of the tetracyclic sesquiterpene longicyclene (**15**)[30,31] (Scheme 3). The only difference was found in the position of the methyl group attached to the cyclopropane ring, at C-3 in **9**, and at C-2 in **15**. Therefore, the new hydrocarbon skeleton is named isolongicyclene.



Scheme 3. Comparison between the carbocyclic structures of the new isolongicyclenone (**9**) and longicyclene (**15**).[30,31]

Compound **10** gave a molecular formula $C_{20}H_{28}O_6$ by HRMS. The ^1H and ^{13}C NMR data were assigned by using the COSY, HETCOR, FLOCK[26] and NOESY correlations (Fig. 1), which indicated that **10** was a decarbonylated analog of **8**. The ^1H NMR spectrum showed signals for one vinylic proton, three protons geminal to acetyloxy group, three acetate methyl groups, three cyclopropane methyne protons, and one vinylic and three tertiary methyl groups. The ^{13}C NMR spectrum showed only twenty signals, thus supporting the extrusion of carbon monoxide. The C-2/H-2 (168.1 Hz), C-5/H-5 (153.4 Hz) and C-11/H-11 (168.3 Hz) coupling constants, obtained by ^1H gated decoupling, evidenced the presence of the three-membered ring.[29] Thus, compound **10** has a norsesquiterpene structure consisting of fused three-, five- and seven-membered rings, which may be defined as a representative of the 1-norpingilonene ring system.

2.3. Biosynthetic implications of longipinene photoreactivity

Taking into account that vulgarone B (**3**) and vulgarone A (**4**) have been found as constituents of the essential oil of *Chrysanthemum vulgare*,[8,9,27] the possibility that a similar photoinduced [1,3]-shift could occur in nature cannot be ruled out. Something similar could occur for longipinene derivatives in *Stevia* species. However, compounds of

types **7**–**10** have not been reported so far from plants of this genus. Therefore, it was of interest to explore if longipinene derivative **2** might undergo photochemical reactions when exposed to solar rays. For this purpose, compound **2** (5 mg) was deposited on a glass surface as a thin layer and exposed to sunlight for 5 h periods during 3 days. The ^{1}H NMR spectrum of the crude material showed the presence of **7** and **8** as the main products in a 47:53 ratio and the complete disappearance of starting material. The presence of tarry materials made the proton methyl signals attributable to **9** and **10** difficult to detect. It is noteworthy that, in general, the acyloxy-1-oxolongipin-2-ene derivatives are isolated in good yields from the roots,[1] which probably are used by the plant as a convenient storage to preserve longipinenes from the sunlight. This hypothesis could be confirmed if compounds of type **7**–**10** were isolated by a careful analysis of the minor and trace constituents of some *Stevia* species, where longipinenes have also been found in the aerial parts.[1]

3. Experimental

3.1. General experimental procedures

Chromatographic separations were performed using Merck silica gel 60 (230–400 mesh ASTM). Melting points are uncorrected. UV spectra were obtained on a Perkin–Elmer Lambda 12 spectrophotometer. IR spectra in $CHCl_3$, were recorded in a Perkin–Elmer 16F PC spectrophotometer. Optical rotations in $CHCl_3$ were determined on a Perkin–Elmer 241 polarimeter. NMR measurements were done on Varian Associates XL-300 GS and Mercury spectrometers from $CDCl_3$ solutions containing TMS as internal standard. The ^{1}H NMR spectra were measured at 300 MHz and the ^{13}C NMR spectra at 75.4 MHz. LRMS were obtained on a Hewlett Packard 5989A spectrometer. HRMS were measured on a VG 7070 high resolution mass spectrometer at the UCR Mass Spectrometry Facility, University of California, Riverside.

3.2. General irradiation procedure

UV irradiations were performed using a Hanau (NK 620, 110 V) low pressure mercury arc lamp contained in a quartz jacket (20 mm o.d.) which was immersed in spectroscopy grade cyclohexane solutions. Previous to irradiation, the solutions were flushed with argon for 20 min; a steady stream of argon was passed through the solution during all irradiations. The reaction container (a glass tube of 23 mm i.d.) was cooled with water at room temperature. Solutions of 30 mg of each compound in 30 mL of cyclohexane were irradiated during 5 min in the case of **2** and during 30 min for **7** and **8**. Cyclohexane was evaporated and the residue separated by column chromatography eluting with hexane–EtOAc (4:1). The relative composition of the crude material was estimated by ^{1}H NMR analysis from the methyl group integrals for each compound.

3.3. Irradiation of 2

Compound **2** was irradiated as described in the general procedure. The product obtained from 10 runs was combined and chromatographed. The first fractions afforded **10** as an oil, which was purified by rechromatography (9 mg, 3%). The following fractions gave a mixture of **7**–**9** (225 mg, 75%) while the last fractions yielded starting material **2** (10 mg, 3%). The mixture was further chromatographed eluting with CH_2Cl_2–EtOAc (19:1) affording **7** as a white solid (168 mg, 56%) and **8** (45 mg, 15%) and **9** (3 mg, 1%) as oils.

3.3.1. (2*S*,5*S*,7*S*,8*R*,9*S*,10*S*,11*R*)-7,8,9-Triacetyloxyvulgarone A (7). Recrystallization from acetone–hexane gave white prisms: mp 130–131°C; $[\alpha]_{589}$=+167, $[\alpha]_{578}$=+174, $[\alpha]_{546}$=+203, $[\alpha]_{436}$=+399, $[\alpha]_{365}$=+823 (*c* 0.15, $CHCl_3$); IR ν_{max}: 1776 (C=O cyclobutanone), 1750 (C=O acetates), 1648 (C=C), 1250 cm^{-1} (C–O); UV λ_{max} 213 (log ϵ 3.69), 283 nm (log ϵ 2.29); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.90 (1H, d, $J_{8,9}$=1.2 Hz, H-9), 5.77 (1H, br s, H-4), 5.20 (1H, dd, $J_{7,8}$=5.8 Hz, $J_{8,9}$=1.2 Hz, H-8), 4.91 (1H, dd, $J_{7,8}$=5.8 Hz, $J_{5,7}$=1.4 Hz, H-7), 3.28 (1H, ddd, $J_{2,11}$=7.5 Hz, $J_{5,11}$=2.5 Hz, $J_{4,11}$=1.3 Hz, H-11), 2.92 (1H, d, $J_{2,11}$=7.5 Hz, H-2), 2.63 (1H, br s, H-5), 2.12 (6H, s, OAc), 2.06 (3H, s, OAc), 1.89 (3H, dd, $J_{4,15}$=2.4 Hz, $J_{5,15}$=1.6 Hz, Me-15), 1.24 (3H, s, Me-14), 1.11 (3H, s, Me-13), 1.05 (3H, s, Me-12); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 203.7 (C-1), 169.9, 169.2, 168.8 (C=O acetates), 138.1 (C-3), 121.7 (C-4), 76.1 (C-8), 74.8 (C-7), 69.6 (C-2), 68.6 (C-9), 64.5 (C-11), 53.9 (C-5), 40.1 (C-6), 35.4 (C-10), 26.7 (Me-13), 25.7 (Me-12), 22.9 (Me-15), 21.9 (Me-14), 20.9, 20.7, 20.7 (Me-acetates); EIMS *m*/*z* (rel. int.) 392 [M]$^+$ (13), 332 (32), 290 (89), 230 (61), 212 (55), 202 (50), 184 (100), 148 (41), 127 (17), 85 (22), 43 (19). HRMS *m*/*z* 392.1846 (calcd for $C_{21}H_{28}O_7$, 392.1835).

3.3.2. (2*S*,5*S*,7*S*,8*R*,9*S*,10*R*,11*R*)-7,8,9-Triacetyloxy-1-oxopingilon-3-ene (8). Oil, $[\alpha]_{589}$=−31, $[\alpha]_{578}$=−32, $[\alpha]_{546}$=−39, $[\alpha]_{436}$=−91, $[\alpha]_{365}$=−246 (*c* 0.16, $CHCl_3$); IR ν_{max}: 1774 (C=O cyclobutanone), 1742 (C=O acetates), 1656 (C=C), 1256 cm^{-1} (C–O); UV λ_{max} 213 (log ϵ 3.64), 286 nm (log ϵ 2.21); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.31 (1H, br s, H-4), 5.27 (1H, d, $J_{7,8}$= 10.4 Hz, H-7), 5.20 (1H, dd, $J_{7,8}$=10.4 Hz, $J_{8,9}$=2.3 Hz, H-8), 5.16 (1H, d, $J_{8,9}$=2.3 Hz, H-9), 3.27 (1H, ddd, $J_{2,11}$=6.8 Hz, $J_{5,11}$=6.7 Hz, $J_{4,11}$=1.5 Hz, H-11), 3.14 (1H, ddd, $J_{2,11}$=6.8 Hz, $J_{2,5}$=5.8 Hz, $J_{2,4}$=0.8 Hz, H-2), 2.36 (1H, dd, $J_{5,11}$=6.7 Hz, $J_{2,5}$=5.8 Hz, H-5), 2.16 (3H, s, OAc), 2.03 (3H, s, OAc), 1.95 (3H, s, OAc), 1.86 (3H, d, $J_{4,15}$=1.6 Hz, Me-15), 1.17 (3H, s, Me-12), 1.14 (3H, s, Me-13), 1.08 (3H, s, Me-14); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 199.7 (C-1), 171.4, 170.7, 170.5 (C=O acetates), 140.7 (C-3), 124.8 (C-4), 77.2 (C-9), 72.1 (C-7), 71.8 (C-8), 63.8 (C-11), 63.6 (C-2), 47.0 (C-10), 42.2 (C-5), 38.2 (C-6), 34.7 (Me-13), 24.4 (Me-14), 24.2 (Me-15), 21.7, 21.6, 21.6 (Me-acetates), 21.2 (Me-12); EIMS *m*/*z* (rel. int.) 392 [M]$^+$ (2), 350 (2), 332 (8), 290 (30), 230 (31), 212 (21), 202 (36), 184 (100), 148 (76), 106 (24), 85 (71), 43 (44). HRMS *m*/*z* 392.1845 (calcd for $C_{21}H_{28}O_7$, 392.1835).

3.3.3. (2*S*,3*S*,4*S*,5*S*,7*S*,8*R*,9*S*,10*R*,11*R*)-7,8,9-Triacetyloxy-1-oxo-isolongicyclene (9). Oil, $[\alpha]_{589}$=+12, $[\alpha]_{578}$= +14, $[\alpha]_{546}$=+14, $[\alpha]_{436}$=+18, $[\alpha]_{365}$=+5 (*c* 0.1, $CHCl_3$); IR ν_{max}: 1744 (C=O cyclopentanone and acetates), 1256 cm^{-1} (C–O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.31 (1H, dd, $J_{7,8}$=10.2 Hz, $J_{8,9}$=2.0 Hz, H-8), 5.24 (1H, d, $J_{8,9}$=2.0 Hz, H-9), 5.13 (1H, d, $J_{7,8}$=10.2 Hz, H-7), 2.17

(3H, s, OAc), 2.15 (1H, br s, H-11), 2.14 (1H, br d, $J_{2,4}$=4.4 Hz, H-4), 2.10 (1H, br s, H-5), 2.04 (3H, s, OAc), 2.00 (1H, dd, $J_{2,4}$=4.4 Hz, $J_{2,11}$=1.5 Hz, H-2), 1.97 (3H, s, OAc), 1.21 (3H, s, Me-15), 1.12 (3H, s, Me-12), 1.06 (3H, s, Me-14), 0.98 (3H, s, Me-13); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 210.4 (C-1), 170.6, 169.8, 169.7 (C=O acetates), 75.5 (C-9), 71.4 (C-7), 68.5 (C-8), 52.4 (C-5), 49.0 (C-11), 46.6 (C-10), 37.4 (C-2), 36.3 (C-6), 32.7 (C-4), 29.6 (Me-13), 29.4 (C-3), 20.6 (Me-14 and Me-acetates), 19.5 (Me-12), 8.5 (Me-15); ^{1}H NMR (C_6D_6, 300 MHz) δ 5.42 (1H, dd, $J_{7,8}$=10.3 Hz, $J_{8,9}$=2.0 Hz, H-8), 5.41 (1H, br s, H-9), 5.30 (1H, d, $J_{7,8}$=10.3 Hz, H-7), 2.09 (1H, br s, H-11), 1.98 (3H, s, OAc), 1.74 (3H, s, OAc), 1.71 (1H, br s, H-5), 1.66 (3H, s, OAc), 1.35 (1H, br d, $J_{2,4}$=4.8 Hz, H-4), 1.27 (1H, dd, $J_{2,4}$=4.8 Hz, $J_{2,11}$=1.3 Hz, H-2), 0.96 (6H, s, Me-14 and Me-15), 0.89 (3H, s, Me-12), 0.72 (3H, s, Me-13); ^{13}C NMR (C_6D_6, 75.4 MHz) δ 208.4 (C-1), 170.2, 169.5, 169.2 (C=O acetates), 75.8 (C-9), 71.5 (C-7), 68.8 (C-8), 52.3 (C-5), 49.1 (C-11), 46.6 (C-10), 37.0 (C-2), 36.2 (C-6), 32.3 (C-4), 29.4 (Me-13), 20.5 (Me-14 and Me-acetates), 20.2 (Me-acetate), 19.5 (Me-12), 8.5 (Me-15). EIMS *m/z* (rel. int.) 392 $[M]^+$(15), 350 (100), 290 (19), 248 (51), 230 (41), 220 (31), 202 (26), 187 (24), 159 (36), 140 (35), 125 (31), 82 (28), 43 (43). HRMS *m/z* 392.1840 (calcd for $C_{21}H_{28}O_7$, 392.1835).

3.3.4. (1*R*,4*R*,6*S*,7*R*,8*S*,9*S*,10*R*)-7,8,9-Triacetyloxy-1-norpingilon-2-ene (10). Oil, $[\alpha]_{589}$=+76, $[\alpha]_{578}$=+79, $[\alpha]_{546}$=+92, $[\alpha]_{436}$=+178, $[\alpha]_{365}$=+335 (*c* 0.21, $CHCl_3$); IR ν_{max}: 1736 (C=O acetates), 1650 (C=C), 1260 cm^{-1} (C–O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.37 (1H, d, $J_{7,8}$=10.5 Hz, H-7), 5.23 (1H, d, $J_{8,9}$=2.2 Hz, H-9), 5.10 (1H, br s, H-4), 4.83 (1H, dd, $J_{7,8}$=10.5 Hz, $J_{8,9}$=2.2 Hz, H-8), 2.20 (3H, s, OAc), 2.00 (3H, s, OAc), 1.92 (3H, s, OAc), 1.85 (1H, dd, $J_{2,5}$=8.0 Hz, $J_{2,11}$=6.1 Hz, H-2), 1.82 (3H, d, $J_{4,15}$=1.5 Hz, Me-15), 1.44 (1H, ddd, $J_{5,11}$=9.2 Hz, $J_{2,11}$=6.1 Hz, $J_{4,11}$=1.5 Hz, H-11), 1.14 (3H, s, Me-13), 1.06 (3H, s, Me-14), 1.02 (1H, dd, $J_{5,11}$=9.2 Hz, $J_{2,5}$=8.0 Hz, H-5), 1.02 (3H, s, Me-12); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 170.9, 170.1, 169.7 (C=O acetates), 141.6 (C-3), 128.8 (C-4), 77.2 (C-9), 72.7 (C-7), 71.4 (C-8), 49.2 (C-10), 36.4 (C-6), 33.6 (Me-13), 33.2 (C-5), 31.9 (C-2), 29.1 (C-11), 27.3 (Me-14), 21.0, 20.7, 20.7 (Me-acetates), 19.6 (Me-12), 17.6 (Me-15); EIMS *m/z* (rel. int.) 364 $[M]^+$ (13), 304 (8), 262 (23), 220 (18), 202 (85), 187 (100), 173 (41), 159 (43), 148 (58), 127 (56), 85 (58), 43 (62). HRMS *m/z* 364.1899 (calcd for $C_{20}H_{28}O_6$, 364.1886).

3.4. Irradiation of 7

Compound **7** was irradiated as described in the general procedure. The product obtained from 3 runs was combined. Its ^{1}H NMR spectrum showed mainly the unchanged compound **7** (70%) together with **9** (30%). Chromatographic separation afforded **9** (6 mg, 7%) and recovered starting material **7** (30 mg, 33%).

3.5. Irradiation of 8

Compound **8** was irradiated as described in the general procedure. The product obtained from 3 runs was combined. Its ^{1}H NMR analysis revealed the presence of **7** (17%), **9** (9%), **10** (37%) and unchanged **8** (37%). Chromatographic separation of this mixture afforded **10** (12 mg, 14%), **7** (7 mg, 8%), starting material **8** (13 mg, 15%) and **9** (3 mg, 3%).

3.6. Monitoring procedure for the irradiation of 2

In order to examine the irradiation time dependence of the product composition, five solutions of **2** (30 mg) in cyclohexane (30 mL) were irradiated separately for: 5, 10, 20, 30, and 60 min. After solvent removal, the residue was dissolved in $CDCl_3$ and subjected to ^{1}H NMR analysis. The product composition was estimated from the signal intensities of the methyl groups in the ^{1}H NMR spectra of the following: Me-13 at δ 1.11 for **7**, Me-12 at δ 1.17 for **8**, Me-15 at δ 1.21 for **9** and Me-12 at δ 1.02 for **10**.

3.7. Sunlight irradiation of 2

A solution of **2** (5 mg) in CH_2Cl_2 was distributed on a watch glass surface (11 cm of diameter) with circular movements. After solvent evaporation compound **2**, deposited as a thin layer, was exposed to solar rays 2250 m over sea level and 19.5°N from the equator (determined with a Garmin 12MAP GPS receiver) for periods of 5 h during 3 days. The product was recovered with CH_2Cl_2 (5 mL), the solvent was evaporated to dryness with a steady stream of argon and the residue was subjected to ^{1}H NMR analysis.

3.8. Molecular modeling calculations

Preliminary structure refinement was achieved by using the MMFF94 force–field calculations as implemented in the PC Spartan Pro molecular modeling program (Wavefunction, Inc., Irvine, CA 92612). The molecular mechanics structures were submitted to geometry optimization using density functional theory at the pBP/DN** level using the same program.

Acknowledgements

Partial financial support from CoNaCyT-México and CYTED-Spain is acknowledged.

References

1. Hernández, L. R.; Catalán, C. A. N.; Joseph-Nathan, P. *Rev. Acad. Colomb. Cienc. Ex. Fis. Nat.* **1998**, *22*, 229–279, available on: [http://www.accefyn.org.co/PubliAcad/Periodicas/83/83(229)/83(nathan).html].
2. Joseph-Nathan, P.; Cerda, C. M.; del Río, R. E.; Román, L. U.; Hernández, J. D. *J. Nat. Prod.* **1986**, *49*, 1053–1060.
3. Román, L. U.; Hernández, J. D.; del Río, R. E.; Bucio, M. A.; Cerda-García-Rojas, C. M.; Joseph-Nathan, P. *J. Org. Chem.* **1991**, *56*, 1938–1940.
4. Román, L. U.; Hernández, J. D.; Cerda-García-Rojas, C. M.; Domínguez-López, R. M.; Joseph-Nathan, P. *J. Nat. Prod.* **1992**, *55*, 577–588.
5. Román, L. U.; Zepeda, L. G.; Morales, N. R.; Hernández, J. D.; Cerda-García-Rojas, C. M.; Joseph-Nathan, P. *J. Nat. Prod.* **1995**, *58*, 1808–1816.
6. Román, L. U.; Zepeda, L. G.; Morales, N. R.; Flores, S.;

Hernández, J. D.; Cerda-García-Rojas, C. M.; Joseph-Nathan, P. *J. Nat. Prod.* **1996**, *59*, 391–395.
7. Román, L. U.; Morales, N. R.; Hernández, J. D.; Cerda-García-Rojas, C. M.; Zepeda, L. G.; Flores-Sandoval, C. A.; Joseph-Nathan, P. *Tetrahedron* **2001**, *57*, 7269–7275.
8. Uchio, Y.; Matsuo, A.; Eguchi, S.; Nakayama, M.; Hayashi, S. *Tetrahedron Lett.* **1977**, 1191–1194.
9. Uchio, Y. *Tetrahedron* **1978**, *34*, 2893–2899.
10. Joseph-Nathan, P.; Meléndez-Rodríguez, M.; Cerda-García-Rojas, C. M.; Catalán, C. A. N. *Tetrahedron Lett.* **1996**, *37*, 8093–8096.
11. (a) Román, L. U.; del Río, R. E.; Hernández, J. D.; Cerda, C. M.; Cervantes, D.; Castañeda, R.; Joseph-Nathan, P. *J. Org. Chem.* **1985**, *50*, 3965–3972. The H-2β/Me-14 NOESY correlation in (2*S*,3*S*,4*R*,5*S*,7*S*,8*R*,9*S*,10*R*,11*R*)-7,8,9-triacetyloxy-2-bromo-1-oxolongipinane, intermediate in the preparation of **2**, revealed that the stereochemistry at C-2 is opposite to that described therein.
12. Houk, K. N. *Chem. Rev.* **1976**, *76*, 1–74.
13. (a) Williams, J. R.; Ziffer, H. *Chem. Commun.* **1967**, 194–195. (b) Williams, J. R.; Ziffer, H. *Chem. Commun.* **1967**, 469–470. (c) Williams, J. R.; Ziffer, H. *Tetrahedron* **1968**, *24*, 6725–6734.
14. Gloor, J.; Schaffner, K.; Jeger, O. *Helv. Chim. Acta* **1971**, *54*, 1864–1869.
15. Williams, J. R.; Sarkisian, G. M. *Chem. Commun.* **1971**, 1564–1565.
16. Engel, P. S.; Schexnayder, M. A.; Ziffer, H.; Seeman, J. I. *J. Am. Chem. Soc.* **1974**, *96*, 924–925.
17. Hurst, J. J.; Whitham, G. H. *J. Chem. Soc.* **1960**, 2864–2869.
18. Erman, W. F. *J. Am. Chem. Soc.* **1967**, *89*, 3828–3841.
19. Schuster, D. I.; Widman, D. *Tetrahedron Lett.* **1971**, 3571–3574.
20. Nakanishi, K.; Goto, T.; Itû, S.; Naton, S.; Nozoe, S. *Natural Products Chemistry*, vol. 1; Academic: London, 1974 p 65.
21. Burkert, U.; Allinger, N. L. *Molecular Mechanics*; *ACS Monograph 177*, American Chemical Society: Washington, DC, 1982.
22. (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098–3100. (b) Perdew, J. P. *Phys. Rev. B* **1986**, *33*, 8822–8824.
23. Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783–2792.
24. Cerda-García-Rojas, C. M.; Zepeda, L. G.; Joseph-Nathan, P. *Tetrahedron Comp. Methodol.* **1990**, *3*, 113–118.
25. Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon: Oxford, 1969 pp 334–337.
26. Reynolds, W. F.; McLean, S.; Perpick-Dumont, M.; Enríquez, R. *Magn. Reson. Chem.* **1989**, *27*, 162–169.
27. Uchio, Y.; Matsuo, A.; Nakayama, M.; Hayashi, S. *Tetrahedron Lett.* **1976**, 2963–2966.
28. Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon: Oxford, 1969 pp 334–341.
29. Günther, H. *NMR Spectroscopy*; Wiley: New York, 1994 pp 505–508.
30. Nayak, U. R.; Dev, S. *Tetrahedron* **1968**, *24*, 4099–4104.
31. Lankhorst, P. P.; van Beek, T. A.; Haasnoot, C. A. G. *Recl. Trav. Chim. Pays-Bas* **1991**, *110*, 470–474.