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Photochemical Rearrangements of Highly Functionalized Longipinene Derivatives

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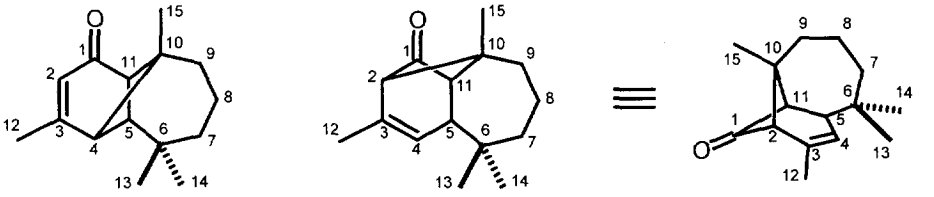
Abstract: Ultraviolet irradiation of 7β,9α-diacetyloxylongipin-2-en-1-one (**3**) affords the vulgarone A derivative **5** and compound **7** which possesses a novel tricyclic sesquiterpene skeleton named pingilonane. The photorearrangements of **3** occur *via* [1,3] sigmatropic shifts of the C_4-C_{10} or of the C_4-C_5 bond, respectively. Similarly, irradiation of 7β,8α,9α-triacetyloxylongipin-2-en-1-one (**4**) affords **6** and **8**. Some biogenetic implications of these transformations are discussed.

The strained tricyclic sesquiterpenes vulgarone A (**2**) and longipin-2-en-1-one (vulgarone B) (**1**) have been found as constituents of the essential oil of *Chrysanthemum vulgare*.[1-3] Since the transformation of **1** into **2** *via* a [1,3] sigmatropic shift can easily be achieved in the laboratory by irradiation with UV light,[2,3] the probability that a similar process could occur in nature can not be ruled out.

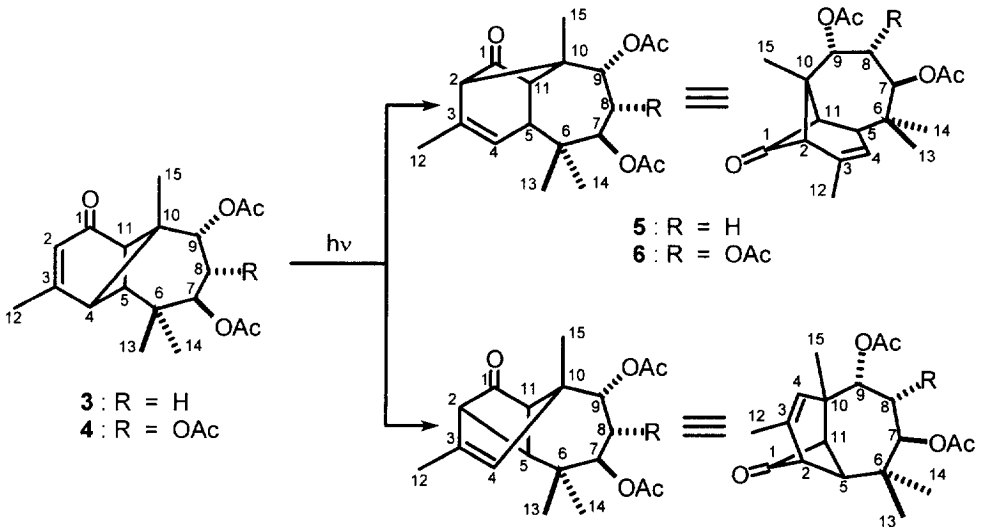


1 **2**

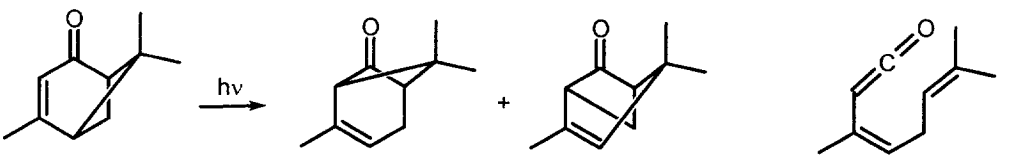
On the other hand, an important number of acyloxylongipin-2-en-1-ones are relevant secondary metabolites in many species of the genus *Stevia*.[4-9] Consequently, the photochemical study of substances such as diacetate **3**[10,11] and triacetate **4**[10,11] can provide new approaches to unusual and highly functionalized tricyclic sesquiterpenes.

Irradiation of diacetate **3** (0.090 mmol) in cyclohexane (30 ml) using a mercury arc lamp (Hanau 110 V) in a quartz tube (20 mm o. d.) for 5 min under an Ar atmosphere, and cooling the reaction container (a glass tube of 23 mm i. d.) with water at room temperature, yielded the two rearranged photoproducts **5**[12] (53%) and **7**[13] (12%). Likewise, irradiation of triacetate **4** (0.077 mmol) in cyclohexane (30 ml) gave **6**[14] (56%) and **8**[15] (15%). In both cases, starting material was recovered (10% and 21%, respectively). The structure of the four products was determined by spectroscopic methods including ^{1}H- and ^{13}C-NMR as well

as 2D correlation diagrams (COSY, HETCOR and FLOCK[16]). The vulgarone A derivatives **5** and **6** are formed by a [1,3] sigmatropic shift of the C_4-C_{10} bond, while photoproducts **7** and **8** are obtained by migration of the C_4-C_5 bond. Compounds **7** and **8** are based on a novel sesquiterpene skeleton that we name *pingilonane*, after a [1,3] exchange of the *lon-gi-pin-ane* syllabic division. It is worth noting that the works[1-3] describing the photochemical transformation of vulgarone B (**1**) into vulgarone A (**2**) do not mention the isolation of the pingilon-3-en-1-one, which most likely was obtained as a minor product of the reaction, since the authors state that the photochemical reaction produced vulgarone A (**2**) in a good yield accompanied by some minor unspecified products.[2]



The photoinduced [1,3] bond shifts observed in the longipinene derivatives **1**, **3** and **4** are formally analogous to those occurring in the conversion of verbenone (**9**) into chrysanthenone (**10**) and 2,4,4-trimethylbicyclo[3.1.1]hept-2-en-6-one (**11**).[17,18] Since formation of chrysanthenone (**10**) occurs with partial optical activity retention,[17] its photochemical racemization is explained by an alternative path which involves the optically inactive species **12** as an intermediate.[18] In our case, if intermediates analogous to **12** were formed, they would be optically active due to the presence of the chiral centers at C_5, C_7 and C_9 in **3** and at C_5, C_7, C_8 and C_9 in **4**. The chiral center at C_5 and the additional seven-membered ring present in **3** and **4** induce the stereochemistry of **5** and **6** and, consequently, formation of stereoisomers with changes at C_2, C_{10} and C_{11} is not to be expected.



Considering the ease of the photochemical rearrangements of **3** and **4** and the widespread distribution of acyloxylongipin-2-en-1-ones in *Stevia*, it is noteworthy that neither vulgarone A derivatives nor pingilonane derivatives have been reported so far from this genus. A close literature examination shows that in general acyloxylongipin-2-en-1-ones are isolated in good yields from the roots,[5,9,19-23] which probably are used by the plant as storage to preserve longipinenes from the sunlight, although in some species such as *Stevia salicifolia*,[4] *S. lemmonia*,[4] *S. berlandieri*,[4] *S. potrerensis*,[5] *S. eupatoria*,[7] and *S. achalensis*[22] longipinenes have also been found in the aerial parts. Therefore, it is feasible that photoproducts like **5-8** should be found there if careful analyses of the minor and trace constituents of such species would be carried out.

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12. **Compound 5:** mp 71-72°C; $[\alpha]_{589}$ +158, $[\alpha]_{578}$ +168, $[\alpha]_{546}$ +197, $[\alpha]_{436}$ +401, $[\alpha]_{365}$ +865 (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1774 (C=O, cyclobutanone), 1731 (C=O, acetates), 1648 (C=C), 1258 cm^{-1} (C-O); ^1H NMR (300 MHz, $CDCl_3$) δ 5.77 (broad s, 1H, H-4), 5.71 (dd, *J*=11.2, 1.2 Hz, 1H, H-9), 4.77 (ddd, *J*=6.3, 1.3 Hz, 1H, H-7), 2.98 (ddd, *J*=7.5, 2.3, 1.3 Hz, 1H, H-11), 2.90 (d, *J*=7.5 Hz, 1H, H-2), 2.55 (broad s, 1H, H-5), 2.12 (s, 3H, OAc), 2.05 (ddd, *J*=14.8, 6.3, 1.2 Hz, 1H, H-8α), 2.03 (s, 3H, OAc), 1.92-1.83 (ddd, *J*=14.8, 11.2, 1.3 Hz, 1H, H-8β), 1.90 (dd, *J*=2.4, 1.6 Hz, 3H, Me-12), 1.13 (s, 3H, Me-15), 1.07 (s, 3H, Me-gem) 0.98 (s, 3H, Me-gem); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 203.9 (C-1), 170.7, 170.2 (C=O, acetates), 137.8 (C-3), 121.9 (C-4), 76.9 (C-7), 68.3 (C-2), 67.6 (C-9), 64.8 (C-11), 54.6 (C-5), 40.0 (C-6), 37.7 (C-10), 32.4 (C-8), 26.8 (Me-gem) 25.1 (Me-gem), 23.1 (Me-12), 21.0,

20.9 (acetates), 19.9 (Me-15); EIMS m/z (rel. int.) 334 $[M]^+$ (2), 292 (9), 274 (17), 232 (59), 214 (26), 204 (15), 199 (11), 163 (17), 150 (76), 135 (100), 121 (57), 108 (32).

13. **Compound 7:** oil; $[\alpha]_{589}$ –25, $[\alpha]_{578}$ –27, $[\alpha]_{546}$ –32, $[\alpha]_{436}$ –67, $[\alpha]_{365}$ –162 (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1772 (C=O, cyclobutanone), 1732 (C=O, acetates), 1660 (C=C), 1254 cm^{-1} (C-O); ^1H NMR (300 MHz, $CDCl_3$) δ 5.13 (broad s, 1H, H-4), 4.90 (dd, *J*=11.1, 1.4 Hz, 1H, H-7), 4.76 (dd, *J*=4.9, 2.2 Hz, 1H, H-9), 3.30 (ddd, *J*=7.5, 2.3, 1.3 Hz, 1H, H-11), 3.11 (ddd, *J*=6.8, 5.8, 0.8, 1H, H-2), 2.28 (dd, *J*=6.7, 5.9 Hz, 1H, H-5), 2.16 (s, 3H, OAc), 2.13 (ddd, *J*=15.2, 11.1, 2.3 Hz, 1H, H-8β), 2.00 (s, 3H, OAc), 1.90 (ddd, *J*=15.1, 4.9, 1.4 Hz, 1H, H-8α), 1.84 (d, *J*=1.5 Hz, 3H, Me-12), 1.12 (s, 6H, Me-gem), 1.09 (s, 3H, Me-15); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 199.7 (C-1), 170.7, 170.2 (acetates), 139.1 (C-3), 125.1 (C-4), 76.1 (C-9), 72.7 (C-7), 63.6 (C-11), 62.3 (C-2), 47.8 (C-10), 41.6 (C-5), 39.4 (C-6), 33.5 (C-8, Me-gem), 23.4 (Me-15), 23.3 (Me-12), 21.1, 21.0 (acetates), 19.5 (Me-gem); EIMS m/z (rel. int.) 334 $[M]^+$ (1), 292 (10), 274 (16), 232 (58), 214 (21), 199 (24), 171 (100), 132 (77).

14. **Compound 6:** mp 130-131°C; $[\alpha]_{589}$ +167, $[\alpha]_{578}$ +174, $[\alpha]_{546}$ +203, $[\alpha]_{436}$ +399, $[\alpha]_{365}$ +823 (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1776 (C=O, cyclobutanone), 1750 (C=O, acetates), 1648 (C=C), 1250 cm^{-1} (C-O); ^1H NMR (300 MHz, $CDCl_3$) δ 5.90 (d, *J*=1.1 Hz, 1H, H-9), 5.77 (broad s, 1H, H-4), 5.2 (dd, *J*=5.8, 1.1 Hz, 1H, H-8), 4.91 (dd, *J*=5.8, 1.3 Hz, 1H, H-7), 3.28 (ddd, *J*=7.5, 2.3, 1.3 Hz, 1H, H-11), 2.92 (d, *J*=7.5 Hz, 1H, H-2), 2.63 (broad s, 1H, H-5), 2.12 (s, 6H, 2OAc), 2.06 (s, 3H, OAc), 1.89 (dd, *J*=2.4, 1.6 Hz, 3H, Me-12), 1.24 (s, 3H, Me-15), 1.11 (s, 3H, Me-gem), 1.05 (s, 3H, Me-gem); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 203.7 (C-1), 169.9, 169.2, 168.8 (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-gem), 25.7 (Me-gem), 22.9 (Me-12), 21.9 (Me-15), 20.9, 20.7 (acetates); EIMS m/z (rel. int.) 392 $[M]^+$ (58), 364 (3), 350 (4), 332 (100), 322 (2), 317 (4), 304 (9).

15. **Compund 8:** oil; $[\alpha]_{589}$ –31, $[\alpha]_{578}$ –32, $[\alpha]_{546}$ –39, $[\alpha]_{436}$ –91, $[\alpha]_{365}$ –246 (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1774 (C=O, cyclobutanone), 1742 (C=O, acetates), 1656 (C=C), 1256 cm^{-1} (C-O); ^1H NMR (300 MHz, $CDCl_3$) δ 5.31 (broad s, 1H, H-4), 5.27 (d, *J*=10.3 Hz, 1H, H-7), 5.20 (dd, *J*=10.4, 2.2 Hz, 1H, H-8), 5.16 (d, *J*=2.3 Hz, 1H, H-9), 3.27 (ddd, *J*=6.8, 1.4 Hz, 1H, H-11), 3.14 (ddd, *J*=6.8, 5.8, 0.8 Hz, 1H, H-2), 2.36 (dd, *J*=6.7, 5.9 Hz, 1H, H-5), 2.12 (s, 3H, OAc), 2.03 (s, 3H, OAc), 1.95 (s, 3H, OAc), 1.86 (d, *J*=1.5 Hz, 3H, Me-12), 1.17 (s, 3H, Me-gem), 1.13 (s, 3H, Me-gem), 1.08 (s, 3H, Me-15); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 199.7 (C-1), 171.4, 170.7, 170.5 (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-gem), 24.4 (Me-15), 24.2 (Me-12), 21.7, 21.6, 21.5 (acetates), 21.2 (Me-gem); EIMS m/z (rel. int.) 392 $[M]^+$ (25), 364 (4), 350 (13), 332 (100), 322 (3), 317 (7), 304 (14).

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