Quirogane, Prenopsane, and Patzcuarane Skeletons Obtained by Photochemically Induced Molecular Rearrangements of Longipinene Derivatives

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Ultraviolet irradiation of (1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-acetyloxy-7-oxolongipin-8-ene (**6**), prepared from longipinene diesters isolated from *Stevia salicifolia*, afforded the new quirogane (**7**) and prenopsane (**8**) derivatives, as the major products, together with the minor secondary photoproduct (1*R*,3*R*,5*R*,8*S*,11*S*)-1-acetyloxy-7-oxopatzcuar-9-ene (**9**), which possesses a novel tricyclic sesquiterpene skeleton. The stereostructures of the new compounds **7**−**9** were mainly determined by NMR techniques including COSY, HSQC, HMBC, and NOESY in combination with molecular modeling obtained by density functional theory calculations. A reaction mechanism accounting for the observed transformations is proposed.

Molecular rearrangements of carbocyclic structures are important tools for the synthetic organic chemists because they allow obtaining, in a single step, new carbocyclic skeletons whose preparation through alternate synthetic methods would involve a more complicated pathway. In particular, photochemical rearrangements have contributed to the development of efficient and selective transformations employed in the preparation of complex bioactive molecules.[1−3] In this sense, natural products, due to their structural versatility and stereochemical variations,[4,5] represent excellent models for experimental and theoretical chemists to conduct these kind of studies.

Several highly functionalized longipinene derivatives are found as the main constituents of many species of the genus *Stevia*.[6] These classes of substances, whose absolute configuration is known,[7] have shown an important tendency to undergo molecular rearrangements due to the strained fused cyclobutane located between a six- and a seven-membered ring.[8−15] These naturally occurring sesquiterpenoids are generally functionalized at C-1 with a carbonyl group and at C-7, C-8, C-9, and C-13 with hydroxyl and/or acyloxy groups.[6]

In previous investigations,[14,15] we have shown that, under ultraviolet irradiation, the longipinene derivative **1** underwent photochemical transformations into **2**−**5** (Scheme 1) owing to the presence of an α,β-unsaturated cyclohexenone moiety with a cyclobutane ring attached to the β-position. To further explore new photochemical rearrangements of longipinene derivatives to obtain unusual and highly functionalized tricyclic sesquiterpenes, we decided to prepare a new longipinene derivative having the α,β-unsaturated carbonyl group at the seven-membered ring instead of at the six-membered ring. This new substrate would have a carbonyl group at C-7 and α,β-unsaturation between C-8 and C-9 and also would possess a four-membered ring attached to the β-position.

In this paper we describe the preparation of (1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-acetyloxy-7-oxolongipin-8-ene (**6**) from the natural longipinene diesters of *Stevia salicifolia* Cav. (Asteraceae), as well as the exploration of its photochemical reactivity. Ultraviolet irradiation of **6** (Scheme 2) afforded (1*S*,3*S*,4*S*,5*S*,8*S*,11*R*)-1-acetyloxy-7-oxoquirog-9-ene (**7**), (1*R*,3*S*,4*R*,5*S*,10*R*,11*R*)-1-acetyloxy-7-oxoprenops-8-ene (**8**), and (1*R*,3*S*,5*R*,8*S*,11*S*)-1-acetyloxy-7-oxopatzcuar-9-ene (**9**). It is pertinent to mention that the latter substance is based on a new carbocyclic skeleton.

During our efforts toward the preparation of starting material **6** for the photochemical studies, new aspects of the chemistry of naturally occurring highly oxygenated longipinene derivatives were found. Furthermore, the results obtained in this work provided new knowledge about the photochemistry of strained sesquiterpenes, which can be useful in the design of synthetic strategies, including those for obtaining new carbocyclic ring systems.

Results and Discussion

Compound **6** was prepared from the longipinantriol **10**, which was easily obtained from the natural longipinendiolone diesters present in the roots of *S. salicifolia*.[16] To achieve such a transformation, it was necessary to protect the secondary hydroxyl groups at C-1 and C-9 in **10**, to oxidize the remaining hydroxyl group at C-7, and, finally, to eliminate the protected hydroxyl group at C-9. Thus, in a first approach, we proceeded to acetylate **10** with Ac_2O (2.15 equiv) in pyridine at −20 °C for 21 days. Chromatographic separation of the crude material afforded the triacetylated derivative **11**[16] in 17% yield, the mixture of diacetylated compounds **12**−**14** (55%), and the monoacetylated products **15**, **16**, and **17** (15%, 7%, and 2%, respectively). Starting material **10** was also recovered (4%). The position of each hydroxyl and/or acetate group in **11**−**17** was evident after comparison of the ^{1}H NMR data of these compounds with those reported for **10**,[16] **11**,[16] and **12**.[13] The ^{1}H and ^{13}C NMR data of **13**−**17** and other molecules obtained during the preparation of **6** are summarized in Tables 1−4 and in the Experimental Section. FLOCK[17] or HMBC correlations were very useful to assign the quaternary carbons C-6 and C-10, since C-6 showed correlations with the proton signals for the *gem*-dimethyl group (Me-12 and Me-13), while C-10 showed a correlation with the proton signal for Me-14. The individual ^{1}H and ^{13}C NMR assignment of Me-12 and Me-13 was established by NOESY correlations from Me-12 to H-4 and from Me-13 to H-11, together with a HETCOR spectrum. In those cases where the NOESY experiments did not allow such proton

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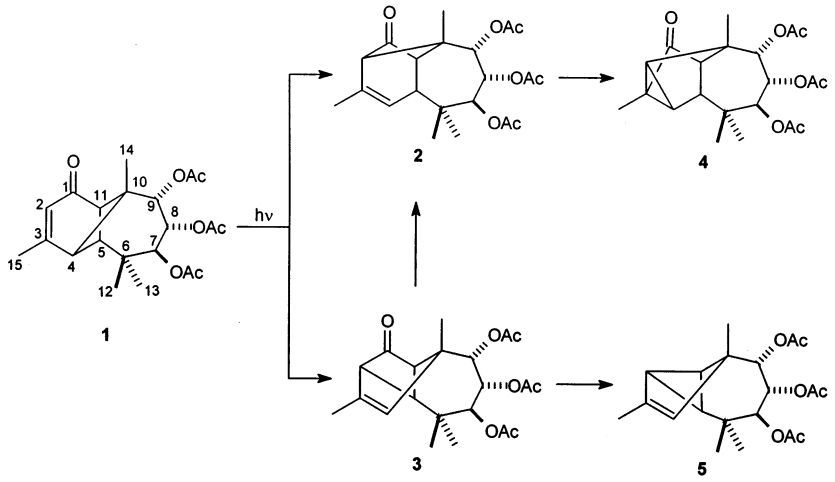
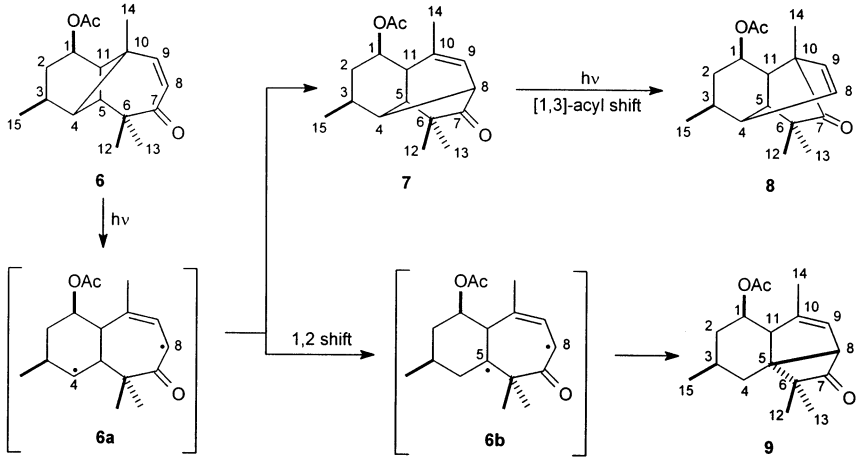
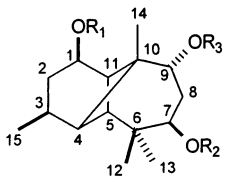
Scheme 1. (4*R*,5*S*,7*S*,8*R*,9*S*,10*R*,11*R*)-7,8,9-Triacetyloxy-1-oxolongipin-2-ene (**1**) and Its Photoproducts **2**−**5**



Scheme 2. (1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-Acetyloxy-7-oxolongipin-8-ene (**6**) and Its Photoproducts **7**−**9**

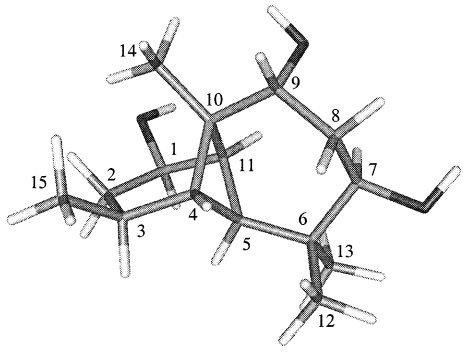


assignments, due to their chemical shift proximity, they were followed by inspection of the HETCOR data taking into account the ^{13}C assignments determined by analogy with the whole series of new and previously reported derivatives.[7−13,16]



10 : $R_1 = R_2 = R_3 = H$
11 : $R_1 = R_2 = R_3 = Ac$
12 : $R_1 = H$; $R_2 = R_3 = Ac$
13 : $R_1 = R_3 = Ac$; $R_2 = H$
14 : $R_1 = R_2 = Ac$; $R_3 = H$
15 : $R_1 = Ac$; $R_2 = R_3 = H$
16 : $R_1 = R_3 = H$; $R_2 = Ac$
17 : $R_1 = R_2 = H$; $R_3 = Ac$

The product ratio for the monoesterified derivatives **15**, **16**, and **17** was 7.5:3.5:1.0, reflecting an important difference in the chemical reactivity of the three secondary hydroxyl groups in compound **10**. The chemical reactivity difference between the hydroxyl groups at C-7 and C-9 was as expected, in agreement with their different orientation, 7-pseudo-equatorial and 9-pseudo-axial, in the twist-chair seven-membered ring conformation previously described for the longipinene system[7] and clearly observed in the minimum energy conformation of triol **10** (Figure 1) obtained by molecular mechanics calculations (MMX)[18] and subsequent geometry optimization using density functional theory computations[19] at the pBP/DN** level of theory. The increased reactivity of the remaining secondary hydroxyl group at C-1 with respect to that at C-7 can be explained by its pseudo-equatorial orientation in the half-chair six-membered ring conformation present in **10** (Figure 1) together with the lack of quaternary carbon atoms at the α-positions, which provided an important steric effect, as is the case of the hydroxyl group at C-7.

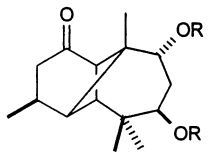


$E_{DFT} = -813.17769$ hartrees

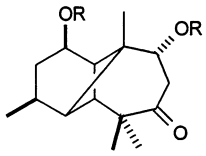
Figure 1. Lowest energy conformation of **10**.

The ^1H NMR spectrum of the mixture of diacetates **12**−**14** indicated that the major product was the 1,7-diacetate **14** (ca. 80%). The mixture was oxidized with

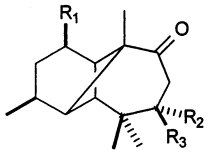
CrO_3/AcOH at room temperature for 2 h, affording a mixture of the isomeric ketones **18**, **19**, and **20** in 68% yield, in a 3.6:1.0:15.4 ratio, respectively, as shown by ^{1}H NMR. Surprisingly, under these oxidizing conditions, the introduction of a hydroxyl group at C-3 in the longipinane system occurred, further affording compound **21** in 8% yield. Its molecular formula $C_{19}H_{28}O_6$ (HREIMS, *m*/*z* 352.1876) was consistent with the presence of an additional hydroxyl group in **21** in comparison to the HREIMS data of **18**−**20**. The introduction of the hydroxyl group at C-3



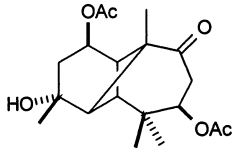
18 : R = Ac
23 : R = H



19 : R = Ac
26 : R = H



20 : $R_1 = R_3 = OAc$; $R_2 = H$
24 : $R_1 = R_3 = OH$; $R_2 = H$
25 : $R_1 = R_2 = OH$; $R_3 = H$



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was also established by the IR broad absorption at 3471 cm^{-1} (OH, br) and the ^{1}H NMR signals at δ_H 2.53 (1H, dd, $J_{2\alpha,2\beta} = 16.6$, $J_{1,2\alpha} = 10.0$ Hz), 1.94 (1H, dd, $J_{2\alpha,2\beta} = 16.6$, $J_{1,2\beta} = 5.0$ Hz), and 5.25 (1H, ddd, $J_{1,2\alpha} = 10.0$, $J_{1,2\beta} = 5.0$, $J_{1,11} = 2.9$ Hz) for the methylene protons H-2α and H-2*β* and the methine proton H-1, respectively. Furthermore, the singlet at δ_H 1.46 for Me-15, in combination with the FLOCK[17] correlation between Me-15 and the quaternary carbon C-3 at δ_C 74.3, was in agreement with the hydroxyl group at C-3. The *R* configuration at C-3 was evident from the NOESY correlation between Me-14 and Me-15, indicating that both methyl groups are located on the *β*-face of the molecule and that the hydroxyl group at C-3 possesses an α-orientation. The presence of a keto group at C-9 was confirmed by the FLOCK[17] correlation between the carbonyl carbon (δ_C 211.6, C-9) and the signal for Me-14 (δ_H 1.26). The individual assignment of the signals for the methylene protons H-8α (3.14, 1H, dd, J = 13.0, 1.5 Hz) and H-8*β* (2.82, 1H, dd, J = 13.0, 7.2 Hz) was achieved from NOESY correlations, since the signal at δ_H 3.14 (H-8α) correlated with H-11 and Me-13. Crystallization of **21** from $CHCl_3$/hexane yielded suitable crystals for an X-ray study. As shown in Figure 2, the X-ray structure confirmed the α-orientation of the hydroxyl group at C-3 in **21**.

Hydrolysis of the acetate groups in the mixture of ketones **18**−**20** with KOH in MeOH/H_2O under reflux for 2 h afforded, after chromatographic separations, the unsaturated compound **22** (60%), ketodiol **23**[16] (9%), and the epimeric mixture of ketodiols **24** and **25** (9% and 5%, respectively). The ^{1}H NMR spectrum of **22** (Table 2) showed two vinylic protons at δ_H 6.05 (H-7) and 5.84 (H-8), which correlated, in the HETCOR diagram, with the sp^2 carbon signals at δ_C 150.3 (C-7) and 126.1 (C-8), respectively, in agreement with the presence of the α,*β*-unsaturated ketone. The signal at δ_H 4.36 (1H, ddd, J = 9.7, 5.3, 3.0 Hz, H-1) was consistent with the presence of a hydroxyl group at C-1. In addition, the IR bands at 3608, 3480 (OH), and 1650

Table 1. ^{1}H NMR Data of Compounds **6**, **13**−**17**, and **19**−**21**[a]

proton	**6**	**13**	**14**	**15**	**16**	**17**	**19**	**20**	**21**
1	5.23 ddd (9.8, 5.5, 2.8)	5.18 ddd (9.6, 5.5, 3.7)	5.19 ddd (9.6, 5.5, 3.4)	5.17 ddd (9.7, 5.4, 3.4)	4.30 ddd (9.4, 5.5, 3.3)	4.27 ddd (9.5, 5.7, 3.1)	5.17 ddd (9.7, 5.5, 3.1)	5.21 ddd (9.7, 5.6, 2.9)	5.25 ddd (10.0, 5.0, 2.9)
2α	2.68 ddd (15.7, 9.8, 9.8)	2.63 ddd (15.7, 9.9, 9.6)	2.64 ddd (15.6, 9.8, 9.6)	2.63 ddd (15.7, 9.8, 9.7)	2.51 ddd (15.2, 9.7, 9.4)	2.56 ddd (15.4, 9.7, 9.5)	2.66 ddd (15.7, 10.0, 9.7)	2.66 ddd (15.5, 9.9, 9.7)	2.53 dd (16.6, 10.0)
2*β*	1.48 ddd (15.7, 7.6, 5.5)	1.45 ddd (15.7, 7.4, 5.5)	1.47 ddd (15.6, 7.5, 5.5)	1.45 ddd (15.7, 7.4, 5.4)	1.53 ddd (15.2, 7.7, 5.5)	1.48 ddd (15.4, 7.6, 5.7)	1.47 ddd (15.7, 7.4, 5.5)	1.56 ddd (15.5, 7.6, 5.6)	1.94 dd (16.6, 5.0)
3	2.18 m	2.14 m (overlap)	2.10 m	2.10 m	2.05 m	2.08 m	2.23 m	2.18 m	
4	2.26 br d (5.5)	1.97 br d (4.5)	1.93 br d (5.4)	1.92 br d (5.2)	1.90 br d (5.4)	1.95 ddd (5.3, 2.0, 1.1)	2.31 br d (5.8)	2.45 br d (5.3)	2.36 br d (5.3)
5	1.26 s	1.05 s	1.02 s	1.01 s	0.90 s (overlap)	0.95 br s	1.14 s	1.17 br s (overlap)	1.86 d (1.2)
7	5.83 d (12.4)	3.73 br d (11.0)	4.98 dd (12.1, 1.7)	3.84 dd (12.1, 1.7)	5.05 dd (12.1, 1.8)	3.75 dd (12.1, 1.9)		4.91 br d (7.5)	4.94 ddd (7.2, 1.5, 1.2)
8α		1.83 ddd (15.0, 3.6, 1.9)	1.77 ddd (14.5, 3.7, 1.7)	1.79 ddd (14.5, 3.6, 1.7)	1.74 ddd (14.4, 3.6, 1.8)	1.84 ddd (15.4, 3.7, 1.9)	2.53 dd (13.1, 4.4)	3.07 dd (13.1, 1.6)	3.14 dd (13.0, 1.5)
8*β*		2.14 ddd (overlap)	2.19 ddd (14.5, 12.1, 3.1)	2.19 ddd (14.5, 12.1, 3.2)	2.16 ddd (14.4, 12.1, 3.0)	2.15 ddd (15.4, 12.1, 3.4)	3.18 dd (13.1, 4.1)	2.82 dd (13.1, 7.5)	2.82 dd (13.0, 7.2)
9	6.54 d (12.4)	4.92 dd (3.6, 3.5)	3.73 dd (3.7, 3.1)	3.71 dd (3.6, 3.2)	3.72 dd (3.6, 3.0)	4.90 dd (3.7, 3.4)	4.98 dd (4.4, 4.1)		
11	2.52 ddd (5.5, 2.8, 1.1)	2.50 ddd (4.5, 3.7, 1.1)	2.53 br m	2.44 br m	2.50 ddd (overlap)	2.41 ddd (5.3, 3.1, 1.3)	2.36 ddd (5.8, 3.1, 1.1)	2.77 ddd (5.3, 2.9, 1.1)	2.80 ddd (5.3, 2.9, 1.3)
12	1.14 s	0.86 s	0.93 s	0.85 s	0.91 s	0.85 s	1.09 s	0.97 s	0.99 s
13	1.14 s	0.98 s	0.87 s	0.97 s	0.84 s	0.97 s	1.00 s	1.07 s	1.13 s
14	1.40 s	1.13 s	1.30 s	1.28 s	1.37 s	1.19 s	1.18 s	1.34 s	1.26 s
15	1.16 d (7.3)	1.11 d (7.2)	1.11 d (7.5)	1.10 d (7.2)	1.11 d (7.3)	1.11 d (7.2)	1.16 d (7.4)	1.16 d (7.4)	1.46 s

[a] Measured in $CDCl_3$ at 300 MHz; δ in ppm from TMS and J values (Hz) in parentheses. The shifts due to substituents at oxygen atoms are given in the Experimental Section.

Table 2. ^{1}H NMR Data of Compounds **22**, **24**, **25**, and **27**−**32**[a]

proton	**22**	**24**	**25**	**27**	**28**	**29**	**30**	**31**	**32**
1	4.36 ddd (9.7, 5.3, 3.0)	4.27 br dd (9.6, 5.7)	4.27 ddd (9.4, 5.7, 3.0)	4.32 ddd (9.5, 5.9, 2.8)	5.28 ddd (9.9, 5.1, 3.1)	2.36 t (4.4)	5.62 ddd (9.7, 5.1, 3.3)	4.39 br m	5.58 ddd (9.8, 5.1, 3.2)
2α	2.65 ddd (15.5, 9.9, 9.7)	2.59 ddd (15.4, 9.7, 9.6)	2.57 ddd (15.4, 9.6, 9.4)	2.60 ddd (15.4, 9.7, 9.5)	2.70 ddd (15.7, 9.9, 9.9)	1.63 dddd (overlap)	2.87 ddd (15.8, 9.9, 9.7)	2.64 ddd (15.4, 9.6, 9.6)	2.83 ddd (15.8, 9.9, 9.8)
2*β*	1.59 ddd (15.5, 7.3, 5.3)	1.55 ddd (15.4, 8.0, 5.7)	1.55 ddd (15.4, 8.0, 5.8)	1.52 ddd (15.4, 7.9, 5.9)	1.58 ddd (15.7, 7.1, 5.1)	1.54 dd (overlap)	1.74 ddd (15.8, 7.2, 5.1)	1.57 ddd (15.4, 7.6, 5.7)	1.69 ddd (15.8, 7.3, 5.1)
3	2.20 m	2.13 m	2.11 m	2.14 m	2.26 m	2.10 m	2.34 m	2.18 m (overlap)	2.29 m (overlap)
4	2.28 br d (5.3)	2.52 br d (overlap)	2.25 br d (5.4)	2.24 br d (5.2)	2.30 br d (5.1)	1.81 br s	2.27 br d (5.0)	2.14 br d (overlap)	2.16 br d (overlap)
5	1.17 br s	1.06 s	1.06 s	1.15 s (overlap)	1.27 br s	1.51 br s	1.35 s	1.13 s	1.26 s
7	6.05 dd (11.8, 2.2)	3.74 br d (8.6, 2.3)	3.72 dd (9.1, 2.2)		6.05 dd (11.9, 2.1)	4.98 d (11.6)	5.35 dd (12.0, 1.5)	5.35 dd (12.0, 1.5)	3.86 br d (11.7)
8α	5.84 d (11.8)	3.00 dd (12.5, 2.3)	2.99 dd (12.3, 9.1)	5.82 d (12.5)	5.85 d (11.9)	1.56 dddd (overlap)	2.24 ddd (overlap)	2.20 ddd (overlap)	2.05 ddd (15.2, 3.7, 1.9)
8*β*		2.92 dd (12.5, 8.6)	2.90 dd (12.3, 2.2)			2.21 ddd (15.3, 11.6, 3.6)	2.46 ddd (14.9, 12.0, 3.1)	2.43 ddd (14.9, 12.0, 3.1)	2.32 ddd (overlap)
9				6.56 d (12.5)		3.64 dd (3.6, 3.3)	5.30 dd (3.3, 3.1)	5.25 dd (3.2, 3.1)	5.25 dd (3.7, 3.4)
11	2.50 ddd (5.2, 3.0, 1.2)	2.52 ddd (overlap)	2.73 ddd (5.4, 3.0, 1.2)	2.43 ddd (5.2, 2.8, 1.2)	2.61 ddd (5.1, 3.1, 1.2)	4.49 br d (4.4)	3.04 br dd (5.0, 3.3)	2.71 dd (4.6, 3.2)	2.90 br m
12	1.08 s	1.02 s	1.00 s	1.13 s	1.09 s	0.96 s	1.21 s	1.15 s	0.95 s
13	1.06 s	1.00 s	1.01 s	1.12 s	1.09 s	1.16 s	1.08 s	1.01 s	1.09 s
14	1.43 s	1.38 s	1.37 s	1.46 s	1.37 s	1.02 s	1.42 s	1.34 s	1.34 s
15	1.15 d (7.1)	1.13 d (7.4)	1.12 d (7.2)	1.16 d (7.1)	1.16 d (7.2)	1.20 d (7.2)	1.25 d (7.3)	1.18 d (7.2)	1.21 d (7.3)

[a] Measured in $CDCl_3$ at 300 MHz; *δ* in ppm from TMS and *J* values (Hz) in parentheses. The shifts due to substituents at oxygen atoms are given in the Experimental Section.

Table 3. ^{1}H NMR Data of Compounds **33**−**41**[a]

proton	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**	**41**
1	5.55 ddd (9.5, 5.6, 3.5)	5.50 ddd (9.5, 5.3, 3.5)	4.37 ddd (9.4, 5.5, 3.4)	4.33 br m	5.23 ddd (overlap)	4.32 ddd (9.4, 5.7, 3.2)	5.23 ddd (9.5, 5.5, 3.4)	5.25 ddd (10.1, 4.8, 3.4)	5.25 ddd (9.4, 5.5, 3.2)
2α	2.81 ddd (15.6, 9.9, 9.5)	2.77 ddd (15.7, 9.8, 9.5)	2.56 ddd (15.5, 9.9, 9.4)	2.60 ddd (15.4, 9.8, 9.8)	2.67 ddd (15.7, 9.8, 9.8)	2.60 ddd (15.4, 9.6, 9.4)	2.67 ddd (15.7, 9.8, 9.5)	2.58 dd (16.3, 10.1)	2.69 ddd (15.8, 9.8, 9.4)
2*β*	1.68 ddd (15.6, 7.3, 5.6)	1.63 ddd (15.7, 7.3, 5.2)	1.57 ddd (15.5, 7.6, 5.5)	1.51 ddd (15.4, 7.7, 5.6)	1.51 ddd (15.7, 7.5, 5.5)	1.54 ddd (15.4, 7.7, 5.7)	1.50 ddd (15.7, 7.3, 5.5)	1.90 dd (16.3, 4.8)	1.52 ddd (15.8, 7.4, 5.5)
3	2.24 m	2.18 m (overlap)	2.12 m	2.13 m	2.15 m (overlap)	2.10 m (overlap)	2.15 m		2.17 m
4	2.09 d (5.3)	1.98 d (5.3)	1.99 br d (5.3)	2.05 br d (overlap)	2.05 br d (overlap)	2.02 br d (overlap)	2.01 br d (5.1)	2.30 br d (5.2)	2.11 br d (5.7)
5	1.21 s	1.11 s	1.02 s	1.04 s	1.13 s (overlap)	1.04 s	1.10 s	1.89 br s	1.15 s (overlap)
7	5.34 dd (12.0, 1.4)	3.88 dd (12.0, 1.4)	5.37 dd (12.1, 1.5)	3.84 br d (12.3)	5.19 dd (11.9, 1.8)	5.21 dd (11.9, 1.7)	5.30 dd (12.1, 1.6)		5.05 dd (12.1, 1.7)
8α	1.97 ddd (14.4, 3.6, 1.4)	1.82 ddd (14.4, 3.4, 1.4)	1.93 ddd (14.3, 3.7, 1.5)	2.05 ddd (overlap)	2.03 ddd (overlap)	2.06 ddd (overlap)	1.93 ddd (14.4, 3.8, 1.6)	3.21 dd (13.3, 4.3)	2.02 ddd (overlap)
8*β*	2.39 ddd (14.4, 12.0, 3.1)	2.19 ddd (overlap)	2.33 ddd (14.3, 12.1, 2.9)	2.29 ddd (15.2, 12.3, 3.3)	2.20 ddd (overlap)	2.24 ddd (14.7, 11.9, 3.2)	2.34 ddd (14.4, 12.1, 3.1)	2.58 dd (13.3, 4.1)	2.26 ddd (14.9, 12.1, 3.1)
9	3.87 dd (3.6, 3.1)	3.76 dd (3.4, 3.2)	3.82 dd (3.7, 2.9)	5.19 dd (3.4, 3.3)	4.90 dd (3.4, 3.4)	4.89 dd (3.5, 3.2)	3.81 dd (3.8, 3.1)	5.02 dd (4.3, 4.1)	5.19 dd (3.7, 3.1)
11	2.80 m (overlap)	2.61 br m	2.56 ddd (overlap)	2.58 ddd (overlap)	2.66 ddd (overlap)	2.56 ddd (overlap)	2.61 br m	2.41 ddd (5.2, 3.4, 1.4)	2.78 br m
12	1.15 s	0.88 s	1.10 s	0.89 s	1.11 s	1.10 s	1.10 s	1.14 s	0.99 s
13	1.01 s	1.00 s	0.93 s	1.01 s	0.97 s	0.95 s	0.96 s	1.08 s	0.95 s
14	1.48 s	1.41 s	1.42 s	1.26 s	1.21 s	1.27 s	1.34 s	1.15 s	1.24 s
15	1.19 d (7.2)	1.15 d (7.3)	1.15 d (7.2)	1.14 d (7.2)	1.15 d (7.3)	1.15 d (7.3)	1.14 d (7.3)	1.50 s	1.16 d (7.0)

[a] Measured in $CDCl_3$ at 300 MHz; *δ* in ppm from TMS and *J* values (Hz) in parentheses. The shifts due to substituents at oxygen atoms are given in the Experimental Section.

Table 4. ^{13}C NMR Data of Compounds **6**, **13**−**17**, **19**−**22**, **24**, **25**, and **27**−**41**[a]

compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-14	C-15
6	76.2	32.9	37.5	50.7	54.0	46.4	205.5	127.7	159.6	41.7	48.2	26.2[b]	26.3[b]	24.2	21.3
13	75.9	33.1	37.3	45.0	56.5	36.5	70.8	35.9	78.0	43.1	40.2	17.5	26.9	21.9	21.5
14	75.9	33.3	37.5	45.4	56.8	35.6	73.1	35.8	75.5	44.2	39.6	18.6	26.7	22.4	21.6
15	76.2	33.3	37.5	45.3	56.9	36.5	69.9	38.9	75.9	44.0	39.3	17.5	27.0	22.5	21.5
16	74.0	35.8	37.8	45.6	57.0	35.7	73.7	35.8	75.8	44.3	42.2	18.8	26.7	22.4	21.8
17	78.4	36.3	37.4	45.3	56.9	36.5	70.9	35.9	74.5	43.3	43.0	17.5	26.9	21.9	21.6
19	75.3	32.8	37.4	45.7	54.4	46.6	210.5	41.7	77.1	43.4	42.1	24.3	22.6	21.9	21.5
20	75.5	32.4	37.4	46.6	56.0	36.6	75.1	43.0	212.1	53.3	43.6	23.6	25.7	17.8	21.2
21	74.3	41.0	74.3	52.3	50.0	36.6	75.4	43.0	211.6	53.2	43.8	23.7	25.7	18.7	30.9
22	74.5	35.9	37.6	44.8	55.2	39.1	150.3	126.1	206.3	52.4	45.1	27.4	27.5	17.9	21.2
24	74.6	35.9	37.6	46.8	56.5	37.3	73.9	47.2	214.3	53.6	46.4	22.0	26.2	17.7	21.3
25	74.5	35.6	37.6	45.9	56.5	37.3	73.8	47.5	214.6	53.6	47.2	21.5	26.2	17.6	21.4
27	74.8	35.8	37.6	51.0	54.3	46.4	205.9	127.4	160.6	41.9	51.3	26.3	26.3	24.2	21.4
28	75.8	32.9	37.6	44.6	54.9	39.2	150.2	126.1	205.8	52.2	42.4	27.4[b]	27.7[b]	18.1	21.1
29	44.2	26.8	38.6	49.7	62.3	37.0	73.8	36.9	75.8	47.5	72.0	26.0	21.7	23.3	19.4
30	77.3	32.9	37.4	45.3	56.2	36.1	74.9	32.5	79.3	43.6	40.8	18.8	26.8	22.4	21.5
31	74.2	36.2	37.4	45.6	56.7	35.9	75.2	32.6	79.7	43.8	43.5	18.8	26.8	22.0	21.6
32	77.6	32.9	37.4	45.1	56.3	36.6	70.8	35.8	80.1	43.6	40.4	17.5	27.0	22.5	21.5
33	77.4	33.2	37.6	45.4	56.6	35.9	75.2	36.2	75.2	44.3	39.8	19.0	26.9	22.8	21.6
34	77.7	33.2	37.5	45.3	56.7	36.5	69.9	39.0	75.7	44.1	39.4	17.5	27.0	22.8	21.5
35	74.0	35.8[b]	37.8	45.7	57.0	36.2	75.9	35.9[b]	75.7	44.4	42.3	19.1	26.9	22.4	21.8
36	74.4	36.4	37.4	45.4	56.9	36.5	71.0	36.0	80.6	43.7	43.2	17.5	26.9	22.0	21.5
37	75.7	33.1	37.3	45.3	56.5	36.0	75.3	32.1	77.5	43.1	40.6	18.9	26.7	21.9	21.5
38	74.4	36.0	37.4	45.5	56.8	36.1	75.5	32.2	77.9	43.4	43.3	18.9	26.8	21.9	21.6
39	75.8	33.3	37.6	45.5	56.8	36.1	75.3	35.8	75.5	44.3	39.7	19.0	26.9	22.5	21.6
40	74.1	41.6	74.6	52.1	48.2	46.4	210.7	41.6	76.6	43.5	42.0	24.3	22.5	22.5	31.1
41	75.7	33.1	37.4	45.3	56.3	35.6	73.0	32.6	79.5	43.5	40.6	18.6	26.7	22.2	21.6

[a] Measured in $CDCl_3$ at 75.4 MHz; δ in ppm from TMS. [b] Tentative assignment. The shifts due to substituents at oxygen atoms are given in the Experimental Section.

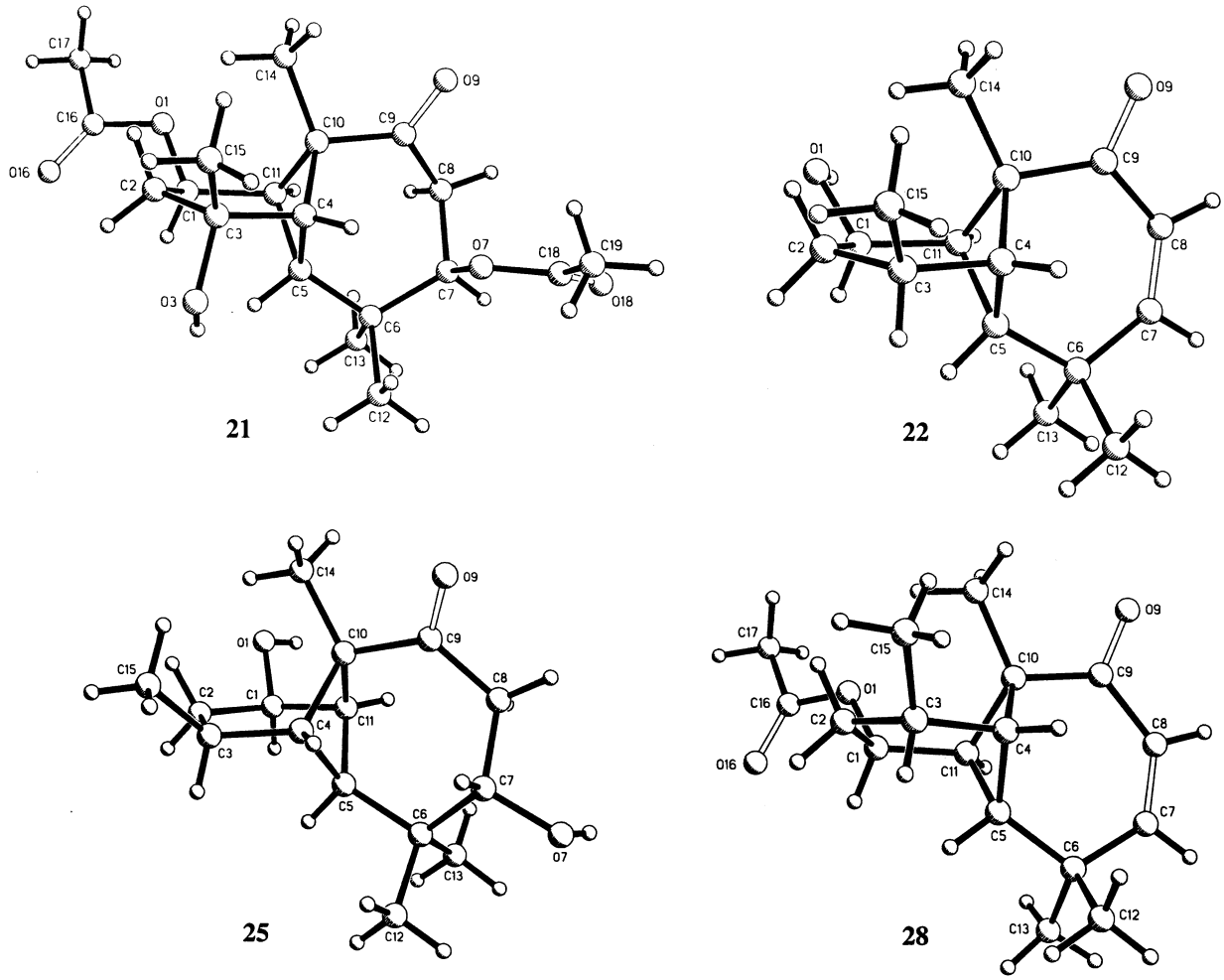
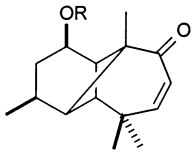


Figure 2. Single-crystal X-ray structures of **21**, **22**, **25**, and **28**.

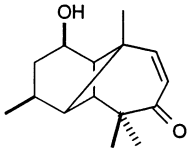
cm^{-1} and the UV absorption at 226 nm supported structure **22**. Crystallization of **22** from ethanol afforded appropriate crystals, which were submitted to an X-ray crystal analysis to confirm the structure (Figure 2).



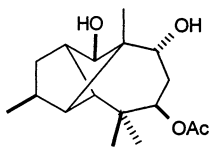
22 : R = H
28 : R = Ac

The IR, HREIMS, and ^{1}H and ^{13}C NMR data as well as 2D NMR correlations of compounds **24** and **25** were very similar to each other. Detailed comparison of the NMR data for these compounds led us to conclude that compound **25** is the C-7 epimer of **24**. Their ^{1}H NMR spectra (Table 2) showed the H-1 and H-7 signals as methine protons geminal to hydroxyl groups. Also, for both compounds, the carbonyl carbon signal correlated with the Me-14, H-4, H-11, and H-7 signals in their HMBC spectra, indicating that the carbonyl group was located at C-9. The above data and the relevant differences found in the ^{1}H NMR signals for the methylene protons H-8α and H-8*β* [for **24**: δ_H 3.00 (1H, dd, J = 12.5, 2.3 Hz, H-8α) and 2.92 (1H, dd, J = 12.5, 8.6 Hz, H-8*β*); for **25**: δ_H 2.99 (1H, dd, J = 12.3, 9.1 Hz, H-8α) and 2.90 (1H, dd, J = 12.3, 2.2 Hz, H-8*β*)] indicated that compounds **24** and **25** are stereoisomers, the only difference being the relative configuration at C-7. NOESY correlations did not provide clear information on the stereochemistry at C-7; however crystallization of compound **25** from $CHCl_3$/hexane yielded crystals, which were subjected to X-ray analysis. As shown in Figure 2, this study provided unambiguous structural confirmation and demonstrated the α-orientation for the hydroxyl group at C-7 in **25**. Consequently, the orientation of this group in **24** is *β*, as in naturally occurring longipinene derivatives.[7] It is noteworthy that in **25** the H-4 (δ_H 2.25, 1H, br d, J = 5.4 Hz) and H-11 (δ_H 2.73, 1H, ddd, J = 5.4, 3.0, 1.2 Hz) signals appeared at the typical chemical shift values of longipinenes, while surprisingly in **24** these signals appeared collapsed as a broad singlet at δ_H 2.52. In **25**, the assignment of the C-4 (δ_C 45.9) and C-11 (δ_C 47.2) signals was achieved from the HETCOR data. In **24**, these assignments were made through an HMBC experiment, where C-4 (δ_C 46.8) correlated with Me-14 and Me-15, while C-11 (δ_C 46.4) correlated only with Me-14.

While the hydroxyl group at C-7 in **24** was easily removed to give the α,*β*-unsaturated ketone **22**, treatment of **26** under the same reaction conditions unexpectedly afforded epimer ketodiol **25** instead of **27**. These findings can be explained by a base-induced transannular 1,3-hydride shift from C-9 to C-7 in **26** to give **25**. The α-orientation of the hydroxyl group at C-7 in ketodiol **25**, clearly observed in Figure 2, is in agreement with the required suprafacial stereochemistry for such hydride migration. Examples of base-induced transannular 1,4- and 1,5-hydride shifts in ketols have been frequently described,[20] while the 1,3-hydride transfer has been scarcely observed.[21]



27



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Treatment of the mixture of ketones **18**−**20** with alumina/H_2O (1.5:1.0 w/w) at 90 °C during 72 h afforded the isomeric α,*β*-unsaturated ketones **6** and **28** in 0.5% and 64% yields, respectively. Under these reaction conditions, partial hydrolysis of the acetate group at C-1 in **28** was observed, also providing the hydrolyzed α,*β*-unsaturated ketone **22** in 14% yield.

The ^{1}H and ^{13}C NMR spectra of **28** (Tables 2 and 4) were similar to those of **22**, except for the presence of an acetate group at C-1 in **28** [H-1 (δ_H 5.28, 1H, ddd, J = 9.9, 5.1, 3.1 Hz); C-1 (δ_C 75.8), OAc (δ_H 2.02, 3H, s; δ_C 170.6, 21.4)]. The molecular structure of **28** was confirmed by X-ray crystallography, whose perspective view is presented in Figure 2.

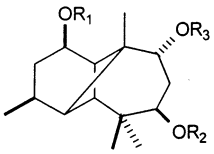
The ^{1}H and ^{13}C NMR data of compound **6** (Tables 1 and 4) showed the expected resonances for the α,*β*-unsaturated ketone: two vinylic protons at δ_H 5.83 (H-8) and 6.54 (H-9), which correlated with signals at δ_C 127.7 (C-8) and 159.6 (C-9) in the HETCOR diagram. The location of the keto group at C-7 was evident from the HMBC correlation between the carbonyl signal at δ_C 205.5 and the *gem*-dimethyl group signal at δ_H 1.14 (6H, s, Me-12, Me-13). The H-1 signal at δ_H 5.23 (1H, ddd, J = 9.8, 5.5, 2.8 Hz) and the singlet at δ_H 2.04 (3H, s, OAc) indicated that the acetyl group remained at the C-1 position. In addition, the IR [1724 (C=O acetate), 1652 cm^{-1} (α,*β*-unsaturated cycloheptenone)] and UV (244 nm) data were in agreement with structure **6**.

Once the preparation of **6** could be completed, it was evident that a very limiting step was the selective generation of the diacetyloxy derivative **13** during the acetylation of **10**. To increase the yield of **13**, we explored variations of the acetylation conditions. In a first attempt, triol **10** was treated with AcCl (2.15 equiv) in acetone at room temperature during 24 h, to afford the mixture of diacetates **12**−**14** (16%), monoacetate **15** (8%), and trace amounts of a new unexpected uruapane[13] derivative **29**. Analysis of the ^{1}H and ^{13}C NMR data of **29** (Tables 2 and 4) as well as its 2D NMR correlations revealed that it possesses an uruapane-type skeleton[13] with secondary hydroxyl groups at C-9 and C-11 and an acetyloxy group at C-7.

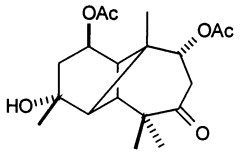
To avoid rearrangement-promoting acid conditions, we used 4-(dimethylamino)pyridine (DMAP) as the neutralizing agent. Thus, when triol **10** was treated with AcCl (2.15 equiv) and DMAP in acetone, a mixture of diacetates **12**−**14** was obtained in 33% yield, together with the triacetyloxy compound **11** (24%), the monoesterified products **15**, **16**, and **17** (20%, 7%, and 2%, respectively), and starting material **10** (12%). Jones oxidation of the mixture **12**−**14** and subsequent elimination of the *β*-acetyloxy group in alumina yielded the desired α,*β*-unsaturated ketone **6** in 6% yield, together with the isomeric ketone **28** (41%), and a mixture of the hydrolyzed products **22** and **27** (20%).

Considering the difference in reactivity among the secondary hydroxyl groups in triol **10**, a more efficient methodology for the preparation of **6** using a protective group was devised. Thus, triol **10** was treated with *p*-nitrobenzoyl chloride (1.4 equiv) in anhydrous pyridine at −4 °C for 24 h to give the tri-, di-, and monoesterified products **30**−**36**, which were separated by column chromatography. From this reaction, the desired C-7 monoester **35** was obtained in 10% yield. Thus, after the hydroxyl group at C-7 was protected as a *p*-nitrobenzoate, acetylation of the remaining hydroxyl groups at C-1 and C-9 was carried out with AcCl under reflux for 10 min, affording triester **37** in very good yields (95%). Subsequent selective hydrolysis of the *p*-nitrobenzoate group was achieved with potassium hydroxide (1.6 N) at room temperature for 7 min to yield diacetate **13** in 63% yield. Minor amounts of diesters **38** (2%) and **39** (1%), monoesters **15** (3%) and **17**

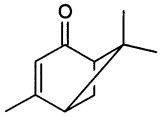
(23%), and triol **10** (2%) were also isolated. The ^{1}H and ^{13}C NMR data of **30**−**39** are listed in Tables 2−4.



30 : $R_1 = R_2 = R_3 = p\text{-}NO_2Bz$
31 : $R_1 = H$; $R_2 = R_3 = p\text{-}NO_2Bz$
32 : $R_1 = R_3 = p\text{-}NO_2Bz$; $R_2 = H$
33 : $R_1 = R_2 = p\text{-}NO_2Bz$; $R_3 = H$
34 : $R_1 = p\text{-}NO_2Bz$; $R_2 = R_3 = H$
35 : $R_1 = R_3 = H$; $R_2 = p\text{-}NO_2Bz$
36 : $R_1 = R_2 = H$; $R_3 = p\text{-}NO_2Bz$
37 : $R_1 = R_3 = Ac$; $R_2 = p\text{-}NO_2Bz$
38 : $R_1 = H$; $R_2 = p\text{-}NO_2Bz$; $R_3 = Ac$
39 : $R_1 = Ac$; $R_2 = p\text{-}NO_2Bz$; $R_3 = H$
41 : $R_1 = R_2 = Ac$; $R_3 = p\text{-}NO_2Bz$



40



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Jones oxidation of the hydroxyl group in **13** gave ketone **19** in 72% yield. Under these conditions, a hydroxyl group was introduced at C-3 in **19** to give compound **40** in 12% yield in a similar way as observed during the oxidation of **20**. The ^{1}H and ^{13}C NMR data of **19** (Tables 1 and 4) confirmed the presence of a carbonyl group (δ_C 210.5) whose position at C-7 was deduced from the HMBC cross-peaks between C-7/Me-12,Me-13. The individual assignment of H-8β at δ_H 3.18 was deduced by NOESY correlation between H-8β/H-4, and consequently the signal at δ_H 2.53 is due to H-8α. The molecular formula of **40**, $C_{19}H_{28}O_6$ (HREIMS, *m*/*z* 352.1888), was consistent with the presence of an additional hydroxyl group as compared to **19**. The ^{1}H and ^{13}C NMR spectra of **40** (Tables 3 and 4) closely resembled those of **19**, except for the signals of H-2α (δ_H 2.58) and H-2β (δ_H 1.90), which appeared as two double doublets, and that of Me-15 (δ_H 1.50), which was observed as a singlet. In the ^{13}C NMR spectra of **40** the signal of C-3 (δ_C 74.6) appeared as a quaternary carbon, which correlated with the proton Me-15 signal in the FLOCK[17] diagram. A NOESY cross-peak from Me-15 to Me-14 indicated the β-Me-15 orientation and, consequently, the α-OH orientation and the *R* configuration at C-3.

Finally, removal of the acetate group at C-9 in **19** with alumina/H_2O afforded the desired α,β-unsaturated ketone **6** in 87% yield, together with the hydrolyzed analogue **27** in 5% yield. The ^{1}H and ^{13}C NMR data of **27** (Tables 2 and 4) are similar to those of **6** except for the absence of the acetyl group signals, the presence of a broad D_2O-exchangeable proton signal (δ_H 1.84), and the shielding of the H-1 signal from δ_H 5.23 in **6** to δ_H 4.32 in **27**. This information indicated that **27** is the 1-hydroxy analogue of **6**.

By using this methodology, the selective preparation of diacetate **13** and ketone **19**, previously obtained in mixtures (**12**−**14** and **18**−**20**) was achieved. Similarly, diacetate **14** and ketone **20** were selectively prepared from the *p*-nitorobenzoyloxy derivative **36**. Acetylation of **36** with AcCl and subsequent selective hydrolysis in the resulting triester **41** afforded diacetate **14**. Jones oxidation of **14** gave ketone **20**. The selective preparation of these compounds allowed us to determine their physical and spectroscopic data. The preparation of diacetate **12**[13] and ketone **18**[16] was previously described.

Acetylation of the hydroxyl groups of **36** was evident from the ^{1}H and ^{13}C NMR data of **41** (Tables 3 and 4). On the other hand, the ^{1}H and ^{13}C NMR data of **20** (Tables 1 and 4) indicated the presence of a carbonyl group at C-9 (δ_C 212.1), which was confirmed by the HMBC correlations of C-9 to H-4, Me-14, and H-7.

Photochemical Reactivity of 6. In view of our interest in inducing new molecular rearrangements and after the successful preparation of **6**, we proceeded to explore its photochemical reactivity. UV irradiation of **6** in cyclohexane using a quartz immersion low-pressure Hg lamp for 15 min resulted in a complex mixture of products, as judged by the ^{1}H NMR spectrum of the crude material. Silica gel chromatography followed by high-performance liquid chromatography (HPLC) using a reversed-phase column and MeOH/H_2O (13:7) as eluent led to the purification of compounds **7**, **8**, and **9** in 5%, 1%, and 3% yields, respectively.

The photorearrangements of the α,β-unsaturated cycloheptenone **6** can be explained considering the mechanism outlined in Scheme 2. The photoisomerization of **6** into the β,γ-unsaturated ketone **7** could proceed via a [1,3]-shift of the C(4)−C(10) bond through the diradical species **6a**. Compound **8** could be a secondary photoproduct derived from the β,γ-unsaturated ketone **7** and formed by a [1,3]-acyl shift.[22] The chiral centers at C-5 and C-11 present in **6** might induce the stereochemistry of **7** and **8**. On the other hand, formation of compound **9** appears to involve a hydrogen migration of H-5 in species **6a** to give species **6b** and subsequent C(5)−C(8) bonding on the β-side of the molecule. The preference in the generation of this diastereoisomer may be due to the lack of the *gem*-dimethyl group steric interaction, which could be relevant if the cyclobutane ring closure occurs on the α-side of the molecule. The proposed mechanism is consistent with those described for analogous photorearrangements, including those of verbenone (**42**)[23−26] and (4*R*,5*S*,7*S*,8*R*,9*S*,10*R*,11*R*)-7,8,9-triacetyloxy-1-oxolongipin-2-ene (**1**).[14,15]

During the preparation of compound **6**, concomitant formation of the isomeric α,β-unsaturated ketone **28** was achieved in a good yield. Therefore, it was interesting to explore if the latter compound might undergo a photorearrangement under the same reaction conditions as those used for **6**. When a cyclohexane solution of compound **28** was irradiated using a quartz immersion low-pressure Hg lamp, no reaction was observed and starting material was recovered even when the irradiation was maintained for 2 h.

The differences in the photochemical behavior between the isomeric ketones **6** and **28** may be due to the differences in the chromophores of both structures. In **6**, the α,β-unsaturated carbonyl group is conjugated to the four-membered ring,[27,28] while in **28**, the cyclobutane is cross-conjugated to the enone system.

Structure Elucidation of Photoproducts 7−9 Using Molecular Modeling and NMR Spectroscopy. The structures of **7**−**9** were mainly determined by analysis of 1D and 2D NMR data as well as by HREIMS. The

Table 5. ^{1}H, ^{13}C NMR and HMBC Data of Compounds **7**−**9**[a]

	compound **7**			compound **8**			compound **9**		
position	δ_H	δ_C	HMBC (C to H)	δ_H	δ_C	HMBC (C to H)	δ_H	δ_C	HMBC (C to H)
1	5.00 ddd (11.8, 4.6, 3.0)	75.5	2, 11	5.25 ddd (11.9, 6.4, 6.0)	75.0	2	5.41 ddd (5.4, 3.4, 2.3)	69.3	2
2α	1.78 ddd (12.3, 4.9, 4.6)	33.3	15	1.75 ddd (12.3, 6.4, 3.5)	32.9	15	2.05 ddd (14.8, 8.8, 5.4)	35.5	4, 15
β	1.59 ddd (12.3, 12.0, 11.8)			1.63 ddd (12.3, 12.1, 11.9)			1.35 ddd (14.8, 7.9, 2.3)		
3	2.05 m (overlap)	31.8	2, 15	1.84 m	33.8	15	1.58 m	25.7	2, 4, 15
4α	2.05 m (overlap)	38.6	2, 9, 15	2.26 m (overlap)	38.3	15	2.00 dd (13.3, 3.0)	33.8	2, 15
β							1.67 dd (13.3, 13.2)		
5	2.02 m (overlap)	48.7	11	1.94 br m	48.2	12, 13		46.0	4, 9, 12, 13
6		48.9	8, 12, 13		48.2	12, 13		61.9	4, 11, 12, 13
7		213.6	12, 13		214.4	12, 13, 14		215.1	12, 13
8	2.76 br m	50.0	4, 9	5.67 ddd (9.5, 4.8, 1.2)	128.6		3.67 br m	74.6	4, 9
9	5.49 br d (6.3)	121.2	14	5.44 dd (9.5, 1.7)	132.2	14	5.38 ddq (2.8, 1.5, 1.5)	123.1	14
10		137.9	5, 11, 14		53.8	14		143.8	14
11	2.53 br t (2.8)	42.1	2, 9, 14	2.25 m (overlap)	41.2	14	2.70 br m	52.1	2, 4, 9, 14
12	1.10 s	26.0	13	1.07 s	26.0	13	1.19 s	20.0	13
13	1.18 s	23.8	12	1.26 s	24.9	12	1.22 s	22.3	14
14	1.70 d (1.4)	23.5	9	1.23 s	18.0		1.72 ddd (2.2, 1.5, 0.8)	14.9	
15	1.06 d (6.6)	20.0	2	0.95 d (6.9)	19.0		0.98 d (6.3)	23.4	2

[a] Measured in $CDCl_3$ at 300 and 75.4 MHz, respctively; δ in ppm from TMS and J values (Hz) in parentheses. The shifts due to substituents at oxygen atoms are given in the Experimental Section.

Table 6. Calculated Dihedral Angles (deg) and Calculated and Observed Vicinal Coupling Constants (Hz) for Compounds **7**−**9**

	compound **7**			compound **8**			compound **9**		
H_x−C−C−H_y	ϕ_{DFT}[a]	J_{calc}[b]	J_{obs}[c]	ϕ_{DFT}[a]	J_{calc}[b]	J_{obs}[c]	ϕ_{DFT}[a]	J_{calc}[b]	J_{obs}[c]
1,2α	−55.3	4.9	4.6	−48.6	5.8	6.4	35.9	5.3	5.4
1,2*β*	−172.5	11.1	11.8	−165.8	10.5	11.9	−77.9	1.8	2.3
1,11	64.4	2.7	3.0	47.4	5.2	6.0	−55.5	2.4	3.4
2α,3	48.2	5.1	4.9	57.4	3.7	3.5	25.7	8.6	8.8
2*β*,3	166.0	11.8	12.0	175.6	12.3	12.1	141.9	8.3	7.9
3,4α	−47.6	4.7	*d*	−65.3	2.1	*d*	−69.9	2.0	3.0
3,4*β*							174.0	12.2	13.2
4,5	54.6	3.6	*d*	62.3	2.4	*d*			
4,8	−55.1	3.5	*d*	−42.1	5.7	4.8			
5,11	−61.0	2.6	*d*	−54.3	3.8	*d*			
8,9	26.7	8.5	6.3	3.9	10.7	9.5	54.4	3.8	2.8
rms		1.0			0.9			0.8	

[a] From density functional theory at the pBP/DN** level.[19] [b] From calculated dihedral angles.[29,30] [c] Measured at 300 MHz in $CDCl_3$. [d] Signal broadening or overlapping precluded the measurements.

correlations found in the NOESY spectra in combination with molecular modeling, and taking into account the absolute configuration of **6**, led to the full stereochemical assignment of the stereogenic centers present in **7**−**9**. The minimum energy conformations were obtained by molecular mechanics calculations (MMX)[18] followed by geometry optimization using density functional theory computation[19] at the pBP/DN** level of theory. The good correspondence between the calculated[29,30] and observed ^{1}H−^{1}H coupling constants (Table 6) allowed us to validate the stereostructures of the new carbocyclic compounds **7**−**9**, as well as their conformation in solution (Figure 3).

Compound **7** had the molecular formula $C_{17}H_{24}O_3$ as deduced from HREIMS in combination with ^{1}H and ^{13}C NMR data (Table 5). Interpretation of its COSY, HETCOR, HSQC, HMBC, and NOESY spectra revealed that **7** has a quirogane-type skeleton.[12] The presence of a *γ*-methyl-*β*,*γ*-unsaturated ketone moiety was evidenced by the IR band at 1726 cm^{-1} and UV absorption at 298 nm. The ^{1}H NMR spectrum showed signals at δ_H 2.76, 5.49, and 1.70 for H-8, H-9, and Me-14, respectively, while the ^{13}C NMR spectrum displayed the corresponding signals at δ_C 213.6, 137.9, 121.2, 50.0, and 23.5 for C-7, C-10, C-9, C-8, and C-14, respectively. The ^{1}H NMR spectra also displayed signals for one proton geminal to an acetate group at δ_H 5.00 (H-1), one acetate methyl group at δ_H 2.05, two methylene and four methine protons, and one secondary and two tertiary methyl groups, in agreement with the proposed structure, which was further supported by the correlations found in the HMBC spectrum of **7** (Table 5). In particular, the C(4)−C(8) bond was confirmed by the COSY interactions between H-4 and H-8 as well as the HMBC correlation between C-4 and H-9 (Table 5). The above data and NOESY interactions between H-2*β* and Me-14; H-1 and H-5; H-5 and Me-12; H-8 and Me-15; H-11 and Me-13; and Me-13 and Me-14

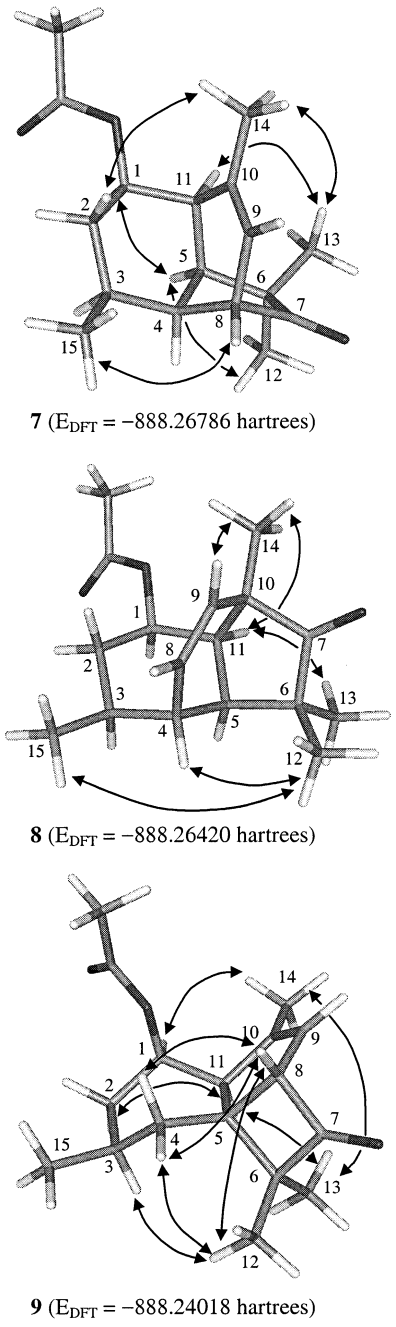

Figure 3. Lowest energy conformation using density functional theory and relevant NOESY correlations for **7**−**9**.

(Figure 3) allowed us to establish the structure of **7** as (1*R*,3*S*,4*S*,5*S*,8*S*,11*R*)-1-acetyloxy-7-oxoquirog-9-ene.

Compound **8** had the molecular formula $C_{17}H_{24}O_3$ as indicated by HREIMS and ^{1}H and ^{13}C NMR data (Table 5). The IR band at 1726 cm^{-1} and UV maximum absorption at 290 nm together with the ^{1}H and ^{13}C NMR data indicated the presence of an α-methyl-*β*,*γ*-unsaturated ketone moiety. The ^{1}H NMR spectra also showed signals due to the same kind of protons as those observed for **7**: one proton geminal to the acetyloxy group, one acetate methyl group, two methylene and four methine protons, and one secondary and two tertiary methyl groups. However, analysis of 2D NMR data demonstrated that compound **8** possesses the same prenopsane[31] skeleton as that of conicumol[32] and prenopsanol.[31] The COSY interaction between H-4 and H-8 in combination with the HMBC cross-peak correlations from C-7 to Me-12, Me-13, and Me-14 (Table 5) were in agreement with the presence of the C(4)−C(8) and C(7)−C(10) bonds. An APT experiment was very useful for the individual assignment of the C-5 and the quaternary carbon C-6 signals, which had a very similar chemical shift at δ_C 48.2. Individual assignments of the methylenic protons at C-2 were confirmed by comparison of the experimental ^{1}H−^{1}H coupling constant values with those obtained from the DFT[19] minimum energy conformation (Table 6). NOESY interactions between H-4 and Me-12 and between H-11 and Me-13 were consistent with the (1*R*,3*S*,4*R*,5*S*,10*R*,11*R*)-1-acetyloxy-7-oxoprenops-8-ene structure of **8** (Figure 3).

HREIMS and NMR data revealed that compound **9** has the $C_{17}H_{24}O_3$ molecular formula. Its IR spectrum showed a band at 1764 cm^{-1}, which supported the existence of a cyclobutanone moiety. The presence of a *γ*-methyl-*β*,*γ*-unsaturated ketone moiety was demonstrated by the UV absorption at λ_{max} 305 nm and by the ^{1}H NMR [δ_H 3.67 (H-8), 5.38 (H-9), 1.72 (Me-14)] and ^{13}C NMR signals [δ_C 215.1 (C-7), 74.6 (C-8), 123.1 (C-9), 143.8 (C-10), 14.9 (Me-14)]. The ^{1}H and ^{13}C NMR spectra (Table 5) also showed signals due to a methine-bearing acetyloxy group [δ_H 5.41 (H-1), 1.97 (OAc); δ_C 69.3 (C-1), 170.3, 21.3 (OAc)], two methylenes [δ_H 2.05 (H-2α), 1.35 (H-2*β*), 2.00 (H-4α), 1.67 (H-4*β*); δ_C 35.5 (C-2), 33.8 (C-4)], one secondary methyl group [δ_H 1.62−1.50 (H-3), 0.98 (Me-15); δ_C 25.7 (C-3), 23.4 (C-15)], and a *gem*-dimethyl group on a quaternary carbon [δ_H 1.19 (Me-12), 1.22 (Me-13); δ_C 61.9 (C-6), 20.0 (C-12), 22.3 (C-13)], a methine [δ_H 2.70 (H-11); δ_C 52.1 (C-11)], and a quaternary carbon δ_C 46.0 (C-5). The individual assignments of the methylene protons H-2α and H-2*β* were confirmed on the basis of calculated and observed ^{1}H−^{1}H coupling constants (Table 6), while those of H-4α and H-4*β* were determined from the NOESY spectrum. Thus, the signal at δ_H 2.00 showed an interaction with the signal for Me-12 and was assigned to H-4α (Figure 3). Consequently, the signal at δ_H 1.67 corresponded to H-4*β*. HMBC correlations between C-5 and H-4, H-9, Me-12, Me-13; between C-6 and H-4, H-11, Me-12, Me-13; and between C-8 and H-4 confirmed the presence of the C(5)−C(4), C(5)−C(6), C(5)−C(8), and C(5)−C(11) bonds. The configuration at C-5 was determined by NOESY interactions between H-4α and H-8 and between H-11 and Me-13 (Figure 3). The above data and a literature search revealed that the structure of **9** has a novel sesquiterpenoid skeleton, which we named patzcuarane. It is noteworthy that the carbocyclic skeleton of **9** resembles that of α- and *β*-panasinsene, main components of the essential oil of the roots of *Panax ginseng*.[33]

Experimental Section

General Experimental Procedures. Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Optical rotations were determined on a Perkin-Elmer 241 polarimeter. UV spectra were obtained on a Perkin-Elmer Lambda 12 spectrophotometer. UV spectra of compounds **30**, **31**, and **33** were measured in CH_3CN because they were insoluble in EtOH. IR spectra were recorded on a Perkin-Elmer 16F PC spectrophotometer. NMR measurements were recorded on Varian Associates XL-300GS and Mercury 300 spectrometers, with the NOESY, HMQC, and HMBC experiments done on the latter instrument. Chemical shifts (*δ*) are given in ppm related to tetramethylsilane. EIMS were recorded at 20 eV on a Hewlett-Packard 5989A spectrometer. HREIMS were measured at the UCR Mass Spectrometry Facility, University of California, Riverside, on a VG 7070 high-resolution mass spectrometer. Column chromatography refers to flash chromatography[34] using the indicated solvent mixture and silica gel Merck grade 60 (230−400 mesh). Anhydrous pyridine was

freshly distilled from a BaO suspension under argon. All commercially available reagents were used as received. All of the solvents employed were spectral or HPLC grade or were distilled from glass prior to use. HPLC separations were carried out employing a semipreparative Varian Dynamax C_{18} (5 mm) reversed-phase column (10 × 250 mm) with a precolumn (10 × 50 mm), using MeOH/H_2O 65:35 (flow rate, 3 mL/min) as the mobile phase on a Varian ProStar 215 solvent delivery module and a Varian ProStar 350 refractive index detector, both controlled by a PC with the Star WS V5 Chromatography Workstation software.

Computational Methods. Preliminary structure refinements were achieved by using MMFF94 force-field calculations as implemented in the PC Spartan Pro molecular modeling program (Wavefunction, Inc., Irvine, CA). Subsequent geometry optimizations were carried out with the same program using density functional theory (DFT) at the pBP/DN** level.

Acetylation of 10 with Ac_2O. A solution of triol **10**[16] (500 mg, 2.0 mmol) in pyridine (3 mL) was treated with a solution of Ac_2O (0.4 mL, 4.2 mmol) in pyridine (1.1 mL). The reaction mixture was stored at −20 °C for 21 days, poured over ice/H_2O, and extracted with EtOAc. The organic layer was washed with dilute HCl, H_2O, aqueous $NaHCO_3$, and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was purified by column chromatography on silica gel. Fractions that eluted with EtOAc/hexane (2:3) gave **11**[16] (130 mg, 17%) and the mixture of **12**−**14** (365.5 mg, 55%). Fractions eluting with EtOAc/hexane (4:1) afforded **15** (90 mg, 15%), **16** (40 mg, 7%), and **17** (10 mg, 2%). Starting material **10** (20 mg, 4%) was recovered from fractions eluting with MeOH/EtOAc (1:19).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1-Acetyloxy-7,9-dihydroxylongipinane (15): white solid; mp 173−175 °C; $[\alpha]_{589}$ +12°, $[\alpha]_{578}$ +14°, $[\alpha]_{546}$ +15°, $[\alpha]_{436}$ +28°, $[\alpha]_{365}$ +46° (*c* 0.17, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3614, 3466 (OH), 1720 (C=O acetate), 1258 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.30 (2H, br s, OH), 2.03 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.8 (C=O acetate), 21.4 (Me-acetate); EIMS *m*/*z* 278 $[M - (H_2O)]^+$ (0.1), 263 (0.4), 236 (5), 218 (8), 203 (12), 175 (32), 121 (43), 107 (42), 95 (100), 81 (23), 69 (30), 55 (13), 43 (43); HRDCIMS (NH_3) *m*/*z* 314.2330 (calcd for $C_{17}H_{28}O_4 + NH_4^+$, 314.2331).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-7-Acetyloxy-1,9-dihydroxylongipinane (16): white solid; mp 168−170 °C; $[\alpha]_{589}$ +13°, $[\alpha]_{578}$ +14°, $[\alpha]_{546}$ +17°, $[\alpha]_{436}$ +32°, $[\alpha]_{365}$ +54° (*c* 0.17, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3604, 3448 (OH), 1726 (C=O acetate), 1260 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 3.12 (2H, br s, OH), 2.08 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 171.0 (C=O acetate), 21.4 (Me-acetate); EIMS *m*/*z* 296 $[M]^+$ (0.1), 278 (1), 254 (2), 236 (13), 218 (19), 203 (45), 175 (51), 159 (43), 123 (61), 109 (84), 95 (94), 81 (46), 69 (71), 55 (37), 43 (100); HRDCIMS (NH_3) *m*/*z* 314.2337 (calcd for $C_{17}H_{28}O_4 + NH_4^+$, 314.2331).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-9-Acetyloxy-1,7-dihydroxylongipinane (17): white solid; mp 136−138 °C; $[\alpha]_{589}$ +15°, $[\alpha]_{578}$ +16°, $[\alpha]_{546}$ +18°, $[\alpha]_{436}$ +32°, $[\alpha]_{365}$ +54° (*c* 0.15, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3612, 3446 (OH), 1720 (C=O acetate), 1252 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.06 (1H, br s, OH), 2.10 (3H, s, OAc), 1.70 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.9 (C=O acetate), 21.3 (Me-acetate); EIMS *m*/*z* 296 $[M]^+$ (0.2), 278 (1), 254 (2), 236 (15), 218 (22), 203 (49), 175 (56), 159 (49), 123 (65), 109 (89), 95 (98), 69 (74), 55 (39), 43 (100); HRDCIMS (NH_3) *m*/*z* 314.2334 (calcd for $C_{17}H_{28}O_4 + NH_4^+$, 314.2331).

Oxidation of the Mixture of 12−14. A solution of the **12**−**14** mixture (700 mg, 2.1 mmol) in glacial AcOH (7 mL) was treated with a solution of CrO_3 (700 mg) in H_2O (1 mL) at 0 °C. The reaction mixture was stored at room temperature for 2 h, poured over ice/H_2O, and extracted with diethyl ether. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, and filtered. After solvent evaporation, the residue was chromatographed on silica gel using EtOAc/hexane (1:4) as eluent to give a mixture of **18**−**20** (475 mg, 68%) and compound **21** (60 mg, 8%).

(1*R*,3*R*,4*S*,5*S*,7*R*,10*R*,11*R*)-1,7-Diacetyloxy-3-hydroxy-9-oxolongipinane (21): colorless crystals ($CHCl_3$/hexane); mp 154−155 °C; $[\alpha]_{589}$ −17°, $[\alpha]_{578}$ −17°, $[\alpha]_{546}$ −21°, $[\alpha]_{436}$ −40°, $[\alpha]_{365}$ −84° (*c* 0.18, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3676, 3471 (OH), 1732 (C=O acetate), 1696 (C=O cycloheptanone), 1240 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.04 (3H, s, OAc), 2.02 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.4, 169.9 (C=O acetates), 21.2, 21.0 (Me-acetates); EIMS *m*/*z* 352 $[M]^+$ (0.3), 292 (1), 250 (6), 232 (16), 217 (8), 189 (16), 161 (14), 135 (12), 95 (18), 69 (8), 55 (7), 43 (100); HREIMS *m*/*z* 352.1876 (calcd for $C_{19}H_{28}O_6$, 352.1886).

Alkaline Hydrolysis of the Mixture of 18−20. A solution of the mixture of **18**−**20** (500 mg, 1.5 mmol) in MeOH (5 mL) was treated with KOH (500 mg) dissolved in 1 mL of H_2O. The reaction mixture was refluxed for 1 h, diluted with ice/H_2O, and extracted with EtOAc. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated and the residue chromatographed over silica gel. Fractions that eluted with EtOAc/hexane (2:3) gave **22** (209 mg, 60%). Fractions eluting with EtOAc/hexane (1:4) afforded **23**[16] (35 mg, 9%) and the mixture of **24** and **25** (85.6 mg, 23%). Subsequent separation of the mixture by column chromatography on silica gel using acetone/EtOAc/CH_2Cl_2 (1:10:10) as eluent gave **24** (35 mg, 9%), **25** (20 mg, 5%), and recovered mixture (35 mg, 9%).

(1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-Hydroxy-9-oxolongipin-7-ene (22): colorless crystals (ethanol); mp 173−174 °C; $[\alpha]_{589}$ +7°, $[\alpha]_{578}$ +7°, $[\alpha]_{546}$ +7°, $[\alpha]_{436}$ −7°, $[\alpha]_{365}$ −168° (*c* 0.15, EtOH); UV (EtOH) λ_{max} (log ϵ) 226 (3.97) nm; IR ν_{max} 3608, 3480 (OH), 1650 (C=C−C=O cycloheptenone), 1260 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 1.84 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4; EIMS *m*/*z* 234 $[M]^+$ (3), 219 (18), 201 (24), 191 (24), 173 (96), 163 (48), 149 (60), 135 (100), 119 (85), 109 (85), 96 (56), 81 (71), 69 (31), 55 (31), 43 (49); HREIMS *m*/*z* 235.1696 (calcd for $C_{15}H_{22}O_2 + H^+$, 235.1698).

(1*R*,3*S*,4*S*,5*S*,7*R*,10*R*,11*R*)-1,7-Dihydroxy-9-oxolongipinane (24): crystalline solid; mp 193−195 °C; $[\alpha]_{589}$ +12°, $[\alpha]_{578}$ +13°, $[\alpha]_{546}$ +15°, $[\alpha]_{436}$ +22°, $[\alpha]_{365}$ +32° (*c* 0.12, EtOH); IR ($CHCl_3$) ν_{max} 3608, 3416 (OH), 1684 (C=O cycloheptanone) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 1.84 (1H, br s, OH), 1.66 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4; EIMS *m*/*z* 252 $[M]^+$ (3), 234 (5), 219 (13), 205 (7), 191 (25), 175 (24), 163 (34), 147 (28), 137 (50), 121 (60), 109 (61), 95 (100), 81 (34), 69 (43), 55 (20), 43 (48); HREIMS *m*/*z* 252.1729 (calcd for $C_{15}H_{24}O_3$, 252.1725).

(1*R*,3*S*,4*S*,5*S*,7*S*,10*R*,11*R*)-1,7-Dihydroxy-9-oxolongipinane (25): colorless crystals ($CHCl_3$/hexane); mp 188−190 °C; $[\alpha]_{589}$ −12°, $[\alpha]_{578}$ −12°, $[\alpha]_{546}$ −14°, $[\alpha]_{436}$ −26°, $[\alpha]_{365}$ −43° (*c* 0.01, EtOH); IR ($CHCl_3$) ν_{max} 3602, 3435 (OH), 1684 (C=O cycloheptanone) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 2.11 (2H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4; EIMS *m*/*z* 252 $[M]^+$ (3), 234 (4), 219 (13), 205 (7), 191 (25), 175 (23), 163 (32), 147 (27), 137 (48), 121 (58), 109 (61), 95 (100), 81 (36), 69 (44), 55 (21), 43 (52); HREIMS *m*/*z* 252.1729 (calcd for $C_{15}H_{24}O_3$, 252.1725).

Reaction of the Mixture of 18−20 with Alumina. A solution of the mixture of **18**−**20** (475 mg, 1.4 mmol) in THF (2 mL) was treated with 2.38 g of activated neutral alumina (Brockmann l, 150 mesh, 58 Å, d = 3.970 from Aldrich Co.). After evaporation of the solvent with a steady stream of nitrogen, H_2O (1.5 mL) was added, and the impregnated alumina was heated at 90 °C for 72 h; addition of H_2O (1.5 mL) every 24 h was necessary. The reaction mixture was brought to room temperature, THF was added, and the alumina was filtered and washed repeatedly with EtOAc. The resulting solution was evaporated, and the residue was chromatographed over silica gel eluting with EtOAc/hexane (4:1) to give a mixture of **6** and **28** (258 mg, 66%), recovered **18**[16] (30 mg, 6%), and **22** (45 mg, 14%). Subsequent separation of the mixture by repeated column chromatography on silica gel using EtOAc/CH_2Cl_2 (1:24) as eluent gave **28** (250 mg, 64%) and **6** (2 mg, 0.5%).

(1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-Acetyloxy-7-oxolongipin-8-ene (6): colorless oil; $[\alpha]_{589}$ +72°, $[\alpha]_{578}$ +76°, $[\alpha]_{546}$ +90°, $[\alpha]_{436}$

+206°, $[\alpha]_{365}$ +555° (*c* 0.18, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 244 (3.32) nm; IR ($CHCl_3$) ν_{max} 1724 (C=O acetate), 1652 (C=C−C=O cycloheptenone), 1252 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.04 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.5 (C=O acetate), 21.3 (Me-acetate); EIMS *m/z* 276 $[M]^+$ (0.2), 234 (3), 216 (3), 201 (10), 188 (11), 173 (34), 145 (100), 131 (24), 119 (40), 96 (11), 81 (6), 67 (6), 55 (4), 43 (28); HREIMS *m/z* 276.1722 (calcd for $C_{17}H_{24}O_3$, 276.1725).

(1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-Acetyloxy-9-oxolongipin-7-ene (28): colorless crystals (acetone/hexane); mp 94−95 °C; $[\alpha]_{589}$ −9°, $[\alpha]_{578}$ −10°, $[\alpha]_{546}$ −13°, $[\alpha]_{436}$ −49°, $[\alpha]_{365}$ −361° (*c* 0.15, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 226 (4.04) nm; IR ($CHCl_3$) ν_{max} 1724 (C=O acetate), 1650 (C=C−C=O cycloheptenone), 1252 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 2.02 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.6 (C=O acetate), 21.4 (Me-acetate); EIMS *m/z* 276 $[M]^+$ (1), 261 (3), 234 (16), 216 (29), 201 (46), 188 (22), 173 (100), 145 (82), 109 (36), 96 (33), 81 (23), 69 (8), 55 (6), 43 (28); HREIMS *m/z* 276.1722 (calcd for $C_{17}H_{24}O_3$, 276.1725).

Acetylation of 10 with AcCl. A solution of **10**[16] (500 mg, 2.0 mmol) in acetone (20 mL) cooled in an ice bath was treated with AcCl (0.3 mL, 4.2 mmol). The reaction mixture was stored at room temperature for 24 h and then quenched and neutralized by addition of an aqueous solution of KOH (6 N). The acetone was removed under reduced pressure, and the crude reaction product was extracted with EtOAc. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under a vacuum to give an oil. After purification of the crude reaction mixture by flash chromatography on silica gel, the mixture of **12**−**14** (104 mg, 16%) was obtained from fractions that eluted with EtOAc/hexane (2:3). Fractions eluting with EtOAc/hexane (4:1) and subsequent flash chromatography with the same eluent gave **15** (46 mg, 18%) and **29** (6 mg, 1%). Starting material **10** (59 mg, 12%) was recovered from fractions eluting with MeOH/EtOAc (1:19).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*S*,11*R*)-7-Acetyloxy-9,11-dihydroxyuruapane (29): colorless oil; $[\alpha]_{589}$ +6°, $[\alpha]_{578}$ +8°, $[\alpha]_{546}$ +8°, $[\alpha]_{436}$ +8°, $[\alpha]_{365}$ +8° (*c* 0.05, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3670, 3436 (OH), 1716 (C=O acetate), 1252 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 2.03 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 171.2 (C=O acetate), 21.4 (Me-acetate); EIMS *m/z* 254 $[M - (CH_2{=}C{=}O)]^+$ (5), 236 (5), 221 (90), 203 (56), 194 (21), 177 (36), 161 (39), 147 (22), 137 (100), 121 (42), 109 (38), 96 (42), 81 (28), 69 (18), 55 (10), 43 (34); HRDCIMS (NH_3) *m/z* 314.2333 (calcd for $C_{17}H_{28}O_4 + NH_4^+$, 314.2331).

Acetylation of 10 with AcCl and 4-(Dimethylamino)-pyridine in Acetone and Subsequent Oxidation and Reaction with Alumina. A solution of **10**[16] (500 mg, 2.0 mmol) and 4-(dimethylamino)pyridine (960 mg, 7.9 mmol) in acetone (15 mL) cooled in an ice bath was slowly treated with a solution of AcCl (0.3 mL, 4.2 mmol) in acetone (5 mL). The reaction mixture was stored at room temperature for 24 h, and the formed precipitate was filtered off and washed with EtOAc. After the acetone was evaporated from the resulting solution, the residue was extracted with EtOAc and worked up as described for the acetylation of **10** with Ac_2O, affording **11**[16] (182 mg, 24%), a mixture of **12**−**14** (218 mg, 33%), **15** (115 mg, 20%), **16** (42 mg, 7%), **17** (11 mg, 2%), and the unreacted **10** (59 mg, 12%). The mixture of **12**−**14** (200 mg, 0.6 mmol) in AcOH (2 mL) was treated with CrO_3 (200 mg) as described above to yield 150 mg (75%) of a mixture of **18**−**20** and 35 mg (17%) of **21**. As described above, the mixture of **18**−**20** (150 mg, 0.5 mmol) in THF (1 mL) treated with neutral alumina (750 mg) and H_2O (0.5 mL, added every 24 h) yielded 7 mg (6%) of **6**, 50 mg (41%) of **28**, 22 mg (15%) of the unreacted **18**,[16] and 21 mg (20%) of a mixture of **22** and **27**.

Esterification of 10 with *p*-Nitrobenzoyl Chloride. A solution of **10**[16] (1 g, 4.0 mmol) and *p*-nitrobenzoyl chloride (1 g, 5.4 mmol) in anhydrous pyridine (25 mL) was stored at 4 °C for 24 h under an argon atmosphere. The reaction mixture was poured over ice/H_2O and extracted with EtOAc. The organic layer was washed with dilute HCl (10%), H_2O, aqueous $NaHCO_3$, and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under a vacuum. The residue was dissolved in $CHCl_3$ and purified by repeated flash chromatography on silica gel. Fractions that eluted with EtOAc/hexane (2:3) gave **30** (570 mg, 21%), a mixture of **31**−**32** (50 mg, 2%), and **33** (302.8 mg, 14%). Fractions eluting with EtOAc/hexane (3:2) afforded **34** (191 mg, 12%), **35** (165 mg, 10%), and **36** (70 mg, 4%). From fractions that eluted with MeOH/EtOAc (1:19), unreacted starting material **10** (96 mg, 10%) was recovered. Subsequent separation of the mixture by flash chromatography on silica gel using EtOAc/CH_2Cl_2 (1:24) was carried out giving **31** (20 mg, 1%) and **32** (29 mg, 1%).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1,7,9-Tri-*p*-nitrobenzoyloxylongipinane (30): yellow crystals (acetone/CH_2Cl_2); mp 150−152 °C; $[\alpha]_{589}$ −62°, $[\alpha]_{578}$ −65°, $[\alpha]_{546}$ −76°, $[\alpha]_{436}$ −136°, $[\alpha]_{365}$ low energy (*c* 0.16, $CHCl_3$); UV (CH_3CN) λ_{max} (log ϵ) 261 (4.33) nm; IR ($CHCl_3$) ν_{max} 1724 (C=O benzoates), 1608 (C=C aromatic), 1530, 1280 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 8.24 and 8.13 (12H, AA′BB′, H-4′, 4″,4‴,6′,6″,6‴ and H-3′,3″,3‴,7′,7″,7‴ *p*-nitrobenzoates); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 164.4, 164.0, 163.8 (C=O benzoates), 150.5, 150.6, 150.6 (C-5′,5″,5‴), 135.8, 135.7, 135.6 (C-2′,2″,2‴), 130.6, 130.5, 130.4 (C-3′,3″,3‴ and C-7′,7″,7‴), 123.6, 123.6, 123.5 (C-4′,4″,4‴ and C-6′,6″,6‴); EIMS *m/z* 671 $[M - (NO)]^+$ (1), 641 (0.1), 367 (30), 324 (4), 260 (3), 217 (29), 200 (66), 150 (100), 120 (48), 95 (9), 65 (5), 44 (6); HRFABMS *m/z* 724.2155 (calcd for $C_{36}H_{35}O_{12}N_3 + Na^+$, 724.2118).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1-Hydroxy-7,9-di-*p*-nitrobenzoyloxylongipinane (31): white solid: mp 222−223 °C; $[\alpha]_{589}$ +68°, $[\alpha]_{578}$ +71°, $[\alpha]_{546}$ +85°, $[\alpha]_{436}$ +188°, $[\alpha]_{365}$ low energy (*c* 0.16, $CHCl_3$); UV (CH_3CN) λ_{max} (log ϵ) 261 (4.44) nm; IR ($CHCl_3$) ν_{max} 3608, 3471 (OH), 1720 (C=O benzoates), 1608 (C=C aromatic), 1530, 1276 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 8.25 and 8.11 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 8.33 (4H, AA′BB′, H-3″,7″ and H-4″,6″ *p*-nitrobenzoate), 1.87 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 164.7, 163.9 (C=O benzoates), 150.5, 150.5 (C-5′,5″), 136.1, 135.7 (C-2′,2″), 130.8, 130.5 (C-3′,3″ and C-7′,7″), 123.6, 123.5 (C-4′,4″ and C-6′,6″); EIMS *m/z* 522 $[M - (NO)]^+$ (2), 385 (6), 367 (5), 341 (6), 324 (6), 235 (5), 218 (93), 203 (18), 175 (47), 159 (16), 150 (100), 120 (31), 95 (14), 81 (5), 65 (1); HRDCIMS (NH_3) *m/z* 570.2449 (calcd for $C_{29}H_{32}O_9N_2 + NH_4^+$, 570.2452).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-7-Hydroxy-1,9-di-*p*-nitrobenzoyloxylongipinane (32): yellow solid; mp 97−99 °C; $[\alpha]_{589}$ −117°, $[\alpha]_{578}$ −123°, $[\alpha]_{546}$ −142°, $[\alpha]_{436}$ −281°, $[\alpha]_{365}$ low energy (*c* 0.19, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 210 (sh) (4.00), 257 (4.35) nm; IR ($CHCl_3$) ν_{max} 3620, 3453 (OH), 1720 (C=O benzoates), 1608 (C=C aromatic), 1530, 1282 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 8.25−8.05 (8H, m, H-3′,3″,7′,7″ and H-4′,4″,6′,6″ *p*-nitrobenzoate), 1.58 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 164.0, 164.0 (C=O benzoates), 150.5, 150.5 (C-5′,5″), 135.8, 135.7 (C-2′,2″), 130.4, 130.3 (C-3′,3″ and C-7′,7″), 123.6, 123.5 (C-4′,4″ and C-6′,6″); EIMS *m/z* 552 $[M]^+$ (0.2), 522 (2), 385 (15), 367 (6), 341 (8), 260 (9), 218 (85), 175 (66), 150 (100), 96 (53), 69 (10), 43 (11); HREIMS *m/z* 552.2104 (calcd for $C_{29}H_{32}O_9N_2 + NH_4^+$, 552.2108).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-9-Hydroxy-1,7-di-*p*-nitrobenzoyloxylongipinane (33): yellow crystals (acetone/hexane); mp 223−225 °C; $[\alpha]_{589}$ −82°, $[\alpha]_{578}$ −86°, $[\alpha]_{546}$ −99°, $[\alpha]_{436}$ −190°, $[\alpha]_{365}$ low energy (*c* 0.16, $CHCl_3$); UV (CH_3CN) λ_{max} (log ϵ) 262 (4.26); IR ($CHCl_3$) ν_{max} 3602, 3480 (OH), 1720 (C=O benzoates), 1608 (C=C aromatic), 1530, 1272 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.25−8.10 (4H, m, H-3′,3″,7′,7″ *p*-nitrobenzoate), 8.35−8.25 (4H, m, H-4′,4″,6′,6″ *p*-nitrobenzoate), 2.15 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 164.2, 164.1 (C=O benzoates), 150.5, 150.4 (C-5′,5″), 136.0, 135.9 (C-2′,2″), 130.6, 130.5 (C-3′,3″ and C-7′,7″), 123.5, 123.4 (C-4′,4″ and C-6′,6″); EIMS *m/z* 522 $[M - (NO)]^+$ (5), 446 (0.7), 385 (4), 343 (9), 296 (4), 235 (5), 218 (47), 203 (35), 189 (24), 176 (67), 161 (43), 150 (98), 137 (35), 121 (100), 107 (37), 96 (31), 65 (6); HRDCIMS (NH_3) *m/z* 570.2445 (calcd for $C_{29}H_{32}O_9N_2 + NH_4^+$, 570.2452).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-7,9-Dihydroxy-1-*p*-nitrobenzoyloxylongipinane (34): yellow oil; $[\alpha]_{589}$ −35°, $[\alpha]_{578}$

−37°, $[\alpha]_{546}$ −43°, $[\alpha]_{436}$ −83°, $[\alpha]_{365}$ low energy (*c* 0.16, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 212 (3.63), 259 (4.10) nm; IR ($CHCl_3$) ν_{max} 3616, 3468 (OH), 1716 (C=O benzoate), 1608 (C=C aromatic), 1530, 1280 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.26 and 8.17 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 2.48 (2H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 164.1 (C=O benzoate), 150.4 (C-5′), 136.1 (C-2′), 130.6 (C-3′ and C-7′), 123.4 (C-4′ and C-6′); EIMS *m/z* 385 $[M - (H_2O)]^+$ (0.2), 373 (0.6), 260 (9), 236 (7), 218 (19), 203 (18), 175 (53), 150 (77), 121 (58), 107 (48), 95 (100), 81 (21), 69 (27), 55 (11), 43 (2); HRDCIMS (NH_3) *m/z* 421.2320 (calcd for $C_{22}H_{29}O_6N + NH_4^+$, 421.2339).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1,9-Dihydroxy-7-*p*-nitrobenzoyloxylongipinane (35): amorphous white solid (CH_2Cl_2/hexane); mp 192 °C; $[\alpha]_{589}$ +10°, $[\alpha]_{578}$ +10°, $[\alpha]_{546}$ +13°, $[\alpha]_{436}$ +29°, $[\alpha]_{365}$ low energy (*c* 0.16, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 210 (sh) (3.83), 259 (4.06) nm; IR ($CHCl_3$) ν_{max} 3604, 3434 (OH), 1718 (C=O benzoate), 1608 (C=C aromatic), 1530, 1280 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.28 and 8.19 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 2.89 (2H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 164.3 (C=O benzoate), 150.5 (C-5′), 136.1 (C-2′), 130.6 (C-3′ and C-7′), 123.5 (C-4′ and C-6′); EIMS *m/z* 385 $[M - (H_2O)]^+$ (2), 373 (2), 284 (4), 257 (6), 236 (17), 218 (24), 203 (39), 175 (48), 150 (56), 137 (100), 120 (67), 109 (71), 95 (57), 81 (34), 69 (55), 57 (27), 43 (49); HRDCIMS (NH_3) *m/z* 421.2346 (calcd for $C_{22}H_{29}O_6N + NH_4^+$, 421.2339).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1,7-Dihydroxy-9-*p*-nitrobenzoyloxylongipinane (36): white crystals (EtOAc/hexane); mp 232−233 °C; $[\alpha]_{589}$ −7°, $[\alpha]_{578}$ −7°, $[\alpha]_{546}$ −8°, $[\alpha]_{436}$ −12°, $[\alpha]_{365}$ low energy (*c* 0.16, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 212 (3.93), 259 (4.24) nm; IR ($CHCl_3$) ν_{max} 3612, 3462 (OH), 1718 (C=O benzoate), 1608 (C=C aromatic), 1530, 1276 (NO_2) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.28 and 8.20 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 1.82 (1H, br s, OH), 1.54−1.48 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 164.3 (C=O benzoate), 150.5 (C-5′), 136.0 (C-2′), 130.6 (C-3′ and C-7′), 123.5 (C-4′ and C-6′); EIMS *m/z* 385 $[M - (H_2O)]^+$ (2), 236 (17), 218 (35), 203 (26), 193 (38), 175 (64), 159 (29), 150 (89), 137 (52), 121 (53), 107 (56), 96 (100), 81 (33), 69 (32), 55 (15), 43 (34); HRDCIMS (NH_3) *m/z* 421.2350 (calcd for $C_{22}H_{29}O_6N + NH_4^+$, 421.2339).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1,9-Diacetyloxy-7-*p*-nitrobenzoyloxylongipinane (37). A solution of **35** (600 mg, 1.5 mmol) in AcCl (3.5 g) was refluxed for 10 min. The AcCl was removed by distillation, and the residue was extracted with EtOAc. The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ and H_2O, dried over anhydrous Na_2SO_4, filtered, and evaporated under vacuum. The residue was chromatographed on silica gel using EtOAc/hexane (1:4) as eluent to give **37** (807 mg, 95%) as a pale yellow oil: $[\alpha]_{589}$ −22°, $[\alpha]_{578}$ −22°, $[\alpha]_{546}$ −25°, $[\alpha]_{436}$ −38°, $[\alpha]_{365}$ low energy (*c* 0.15, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 258 (4.17) nm; IR ($CHCl_3$) ν_{max} 1732 (C=O acetate), 1718 (C=O benzoate), 1608 (C=C aromatic), 1530, 1282 (NO_2), 1258 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.28 and 8.16 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 2.17 (3H, s, OAc), 2.06 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 171.2, 170.6 (C=O acetates), 163.9 (C=O benzoate), 150.5 (C-5′), 136.0 (C-2′), 130.5 (C-3′ and C-7′), 123.5 (C-4′ and C-6′), 21.4, 21.2 (Me-acetates); EIMS *m/z* 457 $[M - (NO)]^+$ (11), 445 (14), 385 (6), 367 (7), 278 (7), 268 (14), 218 (55), 200 (46), 120 (100), 95 (16), 43 (14); HRDCIMS (NH_3) *m/z* 505.2569 (calcd for $C_{26}H_{33}O_8N + NH_4^+$, 505.2550).

Alkaline Hydrolysis of 37. A solution of **37** (600 mg, 1.2 mmol) in MeOH (38 mL) was treated with a 1.6 N solution of KOH (7.5 mL). The reaction mixture was stored at room temperature for 7 min and then neutralized by addition of dilute HCl (20%). The MeOH was evaporated, and the residue was extracted with EtOAc. The organic layer was washed with H_2O, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum, and the residue was flash chromatographed on silica gel. Fractions that eluted with EtOAc/hexane (2:3) gave unreacted **37** (30 mg, 5%), **39** (7.5 mg, 1%), a mixture of **13** and **38** (295 mg), and **17** (84.5 mg, 23%). Fractions eluting with EtOAc afforded **15** (12.5 mg, 3%), and fractions eluting with MeOH/EtOAc (1:19) gave **10** (7.3 mg, 2%). Subsequent separation of the mixture by flash chromatography on silica gel using acetone/EtOAc/CH_2Cl_2 (1:6:14) gave **13** (263 mg, 63%) and **38** (13 mg, 2%).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1,9-Diacetyloxy-7-hydroxylongipinane (13): colorless oil; $[\alpha]_{589}$ +8°, $[\alpha]_{578}$ +9°, $[\alpha]_{546}$ +10°, $[\alpha]_{436}$ +19°, $[\alpha]_{365}$ +35° (*c* 0.35, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3612, 3480 (OH), 1728 (C=O acetate), 1254 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.09 (3H, s, OAc), 2.03 (3H, s, OAc), 1.49 (1H, s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.8, 170.6 (C=O acetates), 21.4, 21.3 (Me-acetates); EIMS *m/z* 296 $[M - (CH_2=C=O)]^+$ (2), 278 (3), 263 (1), 236 (13), 218 (45), 203 (24), 185 (19), 175 (75), 159 (48), 147 (34), 133 (36), 123 (42), 107 (40), 96 (100), 81 (21), 69 (18), 55 (9), 43 (47); HRDCIMS (NH_3) *m/z* 356.2437 (calcd for $C_{19}H_{30}O_5 + NH_4^+$, 356.2437).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-9-Acetyloxy-1-hydroxy-7-*p*-nitrobenzoyloxylongipin-ane (38): pale yellow oil; $[\alpha]_{589}$ −13°, $[\alpha]_{578}$ −13°, $[\alpha]_{546}$ −14°, $[\alpha]_{436}$ −22°, $[\alpha]_{365}$ low energy (*c* 0.13, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 212 (sh) (3.82), 259 (4.04) nm; IR ($CHCl_3$) ν_{max} 3606, 3504 (OH), 1732 (C=O acetate and benzoate), 1608 (C=C aromatic), 1530, 1282 (NO_2), 1254 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.29 and 8.16 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 2.22 (3H, s, OAc), 1.65 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 171.4 (C=O acetate), 164.0 (C=O benzoate), 150.5 (C-5′), 136.0 (C-2′), 130.6 (C-3′ and C-7′), 123.6 (C-4′ and C-6′), 21.3 (Me-acetate); EIMS *m/z* 446 $[M + 1]^+$ (0.2), 415 (2), 403 (7), 236 (35), 218 (100), 175 (77), 150 (57), 120 (61), 95 (51), 81 (33), 69 (25), 43 (46); HRDCIMS (NH_3) *m/z* 463.2458 (calcd for $C_{24}H_{31}O_7N + NH_4^+$, 463.2444).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1-Acetyloxy-9-hydroxy-7-*p*-nitrobenzoyloxylongipinane (39): pale yellow oil; $[\alpha]_{589}$ −10°, $[\alpha]_{578}$ −10°, $[\alpha]_{546}$ −12°, $[\alpha]_{436}$ −19°, $[\alpha]_{365}$ low energy (*c* 0.04, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 212 (sh) (3.80), 259 (3.95) nm; IR ($CHCl_3$) ν_{max} 3250 (OH), 1720 (C=O acetate and benzoate), 1608 (C=C aromatic), 1530, 1280 (NO_2), 1258 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.30 and 8.19 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 2.05 (3H, s, OAc), 1.60 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.8 (C=O acetate), 164.2 (C=O benzoate), 150.5 (C-5′), 136.1 (C-2′), 130.6 (C-3′ and C-7′), 123.6 (C-4′ and C-6′), 21.5 (Me-acetate); EIMS *m/z* 445 $[M]^+$ (0.1), 415 (1), 385 (1), 343 (3), 236 (7), 218 (51), 203 (35), 176 (65), 159 (45), 150 (46), 121 (100), 107 (51), 95 (45), 81 (20), 69 (27), 43 (33); HRDCIMS (NH_3) *m/z* 463.2434 (calcd for $C_{24}H_{31}O_7N + NH_4^+$, 463.2444).

Oxidation of 13. Using the procedure described above, compound **13** (100 mg, 0.3 mmol) in AcOH (1 mL) was treated with CrO_3 (100 mg) to yield 72 mg (72%) of **19** and 13 mg (12%) of **40**.

(1*R*,3*S*,4*S*,5*S*,9*R*,10*R*,11*R*)-1,9-Diacetyloxy-7-oxolongipinane (19): colorless oil; $[\alpha]_{589}$ +1°, $[\alpha]_{578}$ +2°, $[\alpha]_{546}$ +3°, $[\alpha]_{436}$ +27°, $[\alpha]_{365}$ +121° (*c* 0.16, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1728 (C=O acetate), 1720 (C=O cycloheptanone), 1228 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.04 (3H, s, OAc), 1.99 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.6, 170.5 (C=O acetates), 21.3, 21.0 (Me-acetates); EIMS *m/z* 336 $[M]^+$ (0.1), 308 (2), 294 (8), 277 (5), 234 (47), 216 (29), 188 (30), 173 (66), 159 (38), 145 (69), 123 (64), 96 (100), 83 (23), 69 (17), 55 (8), 43 (83); HRDCIMS (NH_3) *m/z* 354.2273 (calcd for $C_{19}H_{28}O_5 + NH_4^+$, 354.2280).

(1*R*,3*R*,4*S*,5*S*,9*R*,10*R*,11*R*)-1,9-Diacetyloxy-3-hydroxy-7-oxolongipinane (40): white solid; mp 143−145 °C; $[\alpha]_{589}$ +12°, $[\alpha]_{578}$ +16°, $[\alpha]_{546}$ +16°, $[\alpha]_{436}$ +36°, $[\alpha]_{365}$ +104° (*c* 0.03, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3674 (OH), 1732 (C=O acetate), 1696 (C=O cycloheptanone), 1244 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 2.08 (3H, s, OAc), 2.01 (3H, s, OAc), 1.75 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.6, 170.4 (C=O acetates), 21.3, 21.1 (Me-acetates); EIMS *m/z* 352 $[M]^+$ (0.2), 334 (0.3), 310 (2), 292 (3), 274 (3), 250 (8), 232 (36), 214 (28), 189 (55), 171 (59), 161 (55), 147

(67), 133 (52), 123 (71), 109 (41), 95 (44), 83 (29), 69 (14), 55 (9), 43 (100); HREIMS *m/z* 352.1888 (calcd for $C_{19}H_{28}O_6$, 352.1886).

Reaction of 19 with Alumina. According to the procedure for the reaction of **18**−**20** with alumina, 185 mg (0.6 mmol) of **19** adsorbed on neutral alumina (925 mg) with H_2O (0.6 mL, added each 24 h) yielded 132 mg (87%) of **6** and 6 mg (5%) of **27**.

(1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-Hydroxy-7-oxolongipin-8-ene (27): white solid; mp 100−102 °C; $[\alpha]_{589}$ −2°, $[\alpha]_{578}$ −2°, $[\alpha]_{546}$ −2°, $[\alpha]_{436}$ −13°, $[\alpha]_{365}$ −83° (*c* 0.10, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 250 (3.82) nm; IR ($CHCl_3$) ν_{max} 3608, 3462 (OH), 1650 (C═C−C═O cycloheptenone), 1258 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 2 and δ 1.84 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4; EIMS *m/z* 234 $[M]^+$ (0.3), 219 (3), 191 (4), 173 (14), 163 (13), 147 (17), 135 (31), 119 (100), 107 (21), 93 (40), 81 (11), 79 (11), 67 (13), 57 (12), 55 (12), 43 (1); HREIMS *m/z* 235.1698 (calcd for $C_{15}H_{22}O_2 + H^+$, 235.1698).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1,7-Diacetyloxy-9-*p*-nitrobenzoyloxylongipinane (41). According to the procedure described for **37**, 300 mg (0.7 mmol) of **36** treated with AcCl (1.5 g) afforded **41** (308.3 mg, 85%) as a yellow oil: $[\alpha]_{589}$ +3°, $[\alpha]_{578}$ +3°, $[\alpha]_{546}$ +4°, $[\alpha]_{436}$ +19°, $[\alpha]_{365}$ low energy (*c* 0.16, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 212 (3.68), 259 (4.06) nm; IR ($CHCl_3$) ν_{max} 1732 (C═O acetate), 1714 (C═O benzoate), 1608 (C═C aromatic), 1530, 1282 (NO_2), 1256 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 3 and δ 8.33 and 8.26 (4H, AA′BB′, H-4′,6′ and H-3′,7′ *p*-nitrobenzoate), 2.00 (3H, s, OAc), 1.98 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.4, 170.3 (C═O acetates), 164.4 (C═O benzoate), 150.3 (C-5′), 136.0 (C-2′), 130.6 (C-3′ and C-7′), 123.5 (C-4′ and C-6′), 21.4, 21.1 (Me-acetates); EIMS *m/z* 457 $[M - (NO)]^+$ (2), 367 (23), 324 (7), 278 (9), 260 (22), 218 (66), 200 (100), 185 (44), 175 (45), 150 (50), 137 (33), 120 (41), 95 (44), 81 (13), 43 (33); HRDCIMS (NH_3) *m/z* 505.2545 (calcd for $C_{26}H_{33}O_8 + NH_4^+$, 505.2550).

(1*R*,3*S*,4*S*,5*S*,7*R*,9*R*,10*R*,11*R*)-1,7-Diacetyloxy-9-hydroxylongipinane (14). According to the procedure described for the alkaline hydrolysis of **37**, 240 mg (0.5 mmol) of **41** in MeOH (15 mL) was treated with a 1.6 N solution of KOH (3 mL) to give 43 mg (26%) of **14** as a pale yellow oil: $[\alpha]_{589}$ 0°, $[\alpha]_{578}$ 0°, $[\alpha]_{546}$ 0°, $[\alpha]_{436}$ +3°, $[\alpha]_{365}$ +8° (*c* 0.15, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3600, 3502 (OH), 1728 (C═O acetate), 1254 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.05 (3H, s, OAc), 2.03 (3H, s, OAc), 1.90 (1H, br s, OH); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.8, 170.8 (C═O acetates), 21.4, 21.3 (Me-acetates); EIMS *m/z* 339 $[M + 1]^+$ (0.1), 296 (0.1), 278 (2), 263 (2), 236 (12), 218 (41), 203 (41), 189 (28), 176 (82), 161 (59), 147 (46), 133 (41), 121 (100), 107 (59), 95 (55), 81 (19), 69 (27), 43 (51); HRDCIMS (NH_3) *m/z* 356.2433 (calcd for $C_{19}H_{30}O_5 + NH_4^+$, 356.2437).

(1*R*,3*S*,4*S*,5*S*,7*R*,10*R*,11*R*)-1,7-Diacetyloxy-9-oxolongipinane (20). According to the procedure described above, 20 mg (0.06 mmol) of **14** in AcOH (0.2 mL) treated with CrO_3 (20 mg) afforded 16 mg (80%) of **20** as colorless crystals (MeOH): mp 156−158 °C; $[\alpha]_{589}$ −22°, $[\alpha]_{578}$ −23°, $[\alpha]_{546}$ −27°, $[\alpha]_{436}$ −52°, $[\alpha]_{365}$ −109° (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) ν_{max} 1732, 1728 (C═O acetates), 1694 (C═O cycloheptanone), 1252 (C−O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1 and δ 2.05 (3H, s, OAc), 2.03 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 4 and δ 170.4, 169.8 (C═O acetates), 21.2, 20.9 (Me-acetates); EIMS *m/z* 336 $[M]^+$ (0.5), 308 (2), 294 (3), 276 (11), 261 (4), 234 (50), 216 (81), 201 (49), 191 (39), 173 (78), 147 (57), 135 (48), 124 (85), 107 (60), 96 (100), 81 (25), 69 (28), 55 (13), 43 (93); HREIMS *m/z* 336.1938 (calcd for $C_{19}H_{28}O_5$, 336.1937).

Single-Crystal X-ray Analysis. Single crystals of **21** and **25** were grown from $CHCl_3$/hexane, while these of **22** and **28** from ethanol and acetone/hexane, respectively. X-ray data of **21**, **22**, **25**, and **28** were collected on a Bruker Smart 6000 CCD diffractometer. A total of 1321 frames were collected at a scan width of 0.3° and an exposure time of 10 s/frame. The frames were processed with the SAINT software package, provided by the diffractometer manufacturer, by using a narrow-frame integration algorithm, and the structure was solved and refined by using the SHELXS-97 program[35] included in the WINGX VI.6 crystallographic software package.[36] In particular, the structure of **21** was solved by searching for a fragment of known geometry by integrated Patterson using the computer program PATSEE[37] in combination with SHELXS-97.[35]

Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

Photochemical Irradiation of (1*R*,3*S*,4*S*,5*S*,10*R*,11*R*)-1-Acetyloxy-7-oxolongipin-8-ene (6). The photoreaction was carried out in a glass tube of 23 mm i.d. cooled with H_2O at room temperature using a Hanau (NK 620, 110V) low-pressure Hg arc immersion lamp (254 nm) contained in a quartz jacket (20 mm o.d.). A solution of **6** (30 mg, 0.1 mmol) in spectroscopic grade cyclohexane (30 mL) was bubbled with argon before (20 min) and during the irradiation. The solution was irradiated for 15 min, and then the solvent was evaporated. After four runs, the combined residue was flash chromatographed on silica gel using EtOAc/hexane (3:17) as eluent separating eight fractions (I−VIII) on the basis of TLC analysis. The ^1H NMR spectrum of the main fraction IV (30 mg, 25%) showed a mixture of three main rearranged compounds. This fraction was dissolved in MeOH and separated by semipreparative reversed-phase HPLC (Varian Dynamax, C_{18}, 5 mm, 10 × 250 mm with a precolumn 5 mm, 10 × 50 mm; MeOH/H_2O (65:35), 3 mL/min; differential refractive index detector) to give **7** (6.1 mg, 5%), **8** (1.7 mg, 1%), and **9** (3.2 mg, 3%).

(1*R*,3*S*,4*S*,5*S*,8*S*,11*R*)-1-Acetyloxy-7-oxoquirog-9-ene (7): colorless oil; $[\alpha]_{589}$ +576°, $[\alpha]_{578}$ +611°, $[\alpha]_{546}$ +717°, $[\alpha]_{436}$ +1528°, $[\alpha]_{365}$ +3678° (*c* 0.05, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 216 (3.77), 298 (2.79) nm; IR ($CHCl_3$) ν_{max} 1726 (C═O cycloheptanone and acetate), 1252 (C−O) cm^{-1}; HPLC t_R 30 min; ^1H NMR ($CDCl_3$, 300 MHz), see Table 5 and δ 2.05 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 5 and δ 170.4 (C═O acetate), 21.5 (Me-acetate); EIMS *m/z* 276 $[M]^+$ (12), 248 (0.1), 233 (0.1), 216 (0.5), 188 (10), 173 (7), 161 (2), 145 (100), 131 (5), 119 (14), 105 (4), 93 (2), 72 (4), 55 (1), 43 (17); HREIMS *m/z* 276.1726 (calcd for $C_{17}H_{24}O_3$, 276.1725).

(1*R*,3*S*,4*R*,5*S*,10*R*,11*R*)-1-Acetyloxy-7-oxoprenops-8-ene (8): colorless oil; $[\alpha]_{589}$ −150°, $[\alpha]_{578}$ −150°, $[\alpha]_{546}$ −186°, $[\alpha]_{436}$ −429°, $[\alpha]_{365}$ −1036° (*c* 0.01, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 210 (3.72), 290 (2.66) nm; IR ($CHCl_3$) ν_{max} 1726 (C═O cycloheptanone and acetate), 1254 (C−O) cm^{-1}; HPLC t_R 42 min; ^1H NMR ($CDCl_3$, 300 MHz), see Table 5 and δ 2.06 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 5 and δ 170.6 (C═O acetate), 21.3 (Me-acetate); EIMS *m/z* 276 $[M]^+$ (10), 248 (0.1), 216 (0.5), 188 (9), 173 (7), 161 (2), 145 (100), 131 (5), 119 (14), 105 (3), 93 (2), 72 (4), 55 (1), 43 (16); HREIMS *m/z* 276.1726 (calcd for $C_{17}H_{24}O_3$, 276.1725).

(1*R*,3*R*,5*R*,8*S*,11*S*)-1-Acetyloxy-7-oxopatzcuar-9-ene (9): colorless oil; $[\alpha]_{589}$ +329°, $[\alpha]_{578}$ +350°, $[\alpha]_{546}$ +412°, $[\alpha]_{436}$ +894°, $[\alpha]_{365}$ +2406° (*c* 0.03, $CHCl_3$); UV (EtOH) λ_{max} (log ϵ) 208 (3.64), 305 (2.47) nm; IR ($CHCl_3$) ν_{max} 1764 (C═O cyclobutanone), 1728 (C═O acetate), 1250 (C−O) cm^{-1}; HPLC t_R 34 min; ^1H NMR ($CDCl_3$, 300 MHz), see Table 5 and δ 1.97 (3H, s, OAc); ^{13}C NMR ($CDCl_3$, 75.4 MHz), see Table 5 and δ 170.3 (C═O acetate), 21.3 (Me-acetate); EIMS *m/z* 234 $[M - (CH_2{=}C{=}O)]^+$ (0.4), 206 (26), 189 (3), 173 (24), 163 (3), 146 (95), 131 (100), 121 (4), 105 (6), 91 (3), 69 (2), 57 (1), 43 (16); HREIMS *m/z* 276.1726 (calcd for $C_{17}H_{24}O_3$, 276.1725).

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Supporting Information Available: Atomic coordinates, bond distances, bond angles, and crystallographic data of compounds **21**, **22**, **25**, and **28** (S1−S17) are available free of charge via the Internet at http://pubs.acs.org.

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