Isoterracinolides A and B, Novel Bishomoditerpene Lactones from *Euphorbia terracina*

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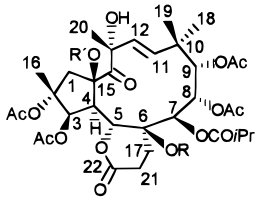
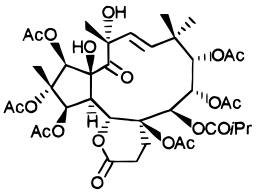
An extract of *Euphorbia terracina* L. has yielded six acylated polyhydroxy terpenoid lactones (**1**−**6**), which all display the C_{22} 17-ethyljatrophane carbon framework. Four of these (**1**−**4**) are δ lactones belonging to the previously described terracinolide type, and two of them (**2**, **3**) are new. Two further new compounds have been named isoterracinolides A (**5**) and B (**6**) and exhibit an eight-membered lactone ring. Another isolated new compound is the jolkinolide-type, *ent*-abietane γ lactone (**7**).

Many species of the spurge family (Euphorbiaceae) are known to exert toxicological effects on animals and humans.[1] When broken or cut, the aerial parts of some species, most particularly those of the genus *Euphorbia*,[2] excrete a milky fluid that causes a number of physiological effects including skin irritation, tumor promotion, and proinflammatory properties.[1] In many cases, these biological responses are due to the presence of specific types of diterpenes, most particularly phorbol derivatives.[3] Other diterpenes with notable biological properties are those displaying the jatrophane framework. The antitumor agent jatrophone, present in certain *Jatropha* species, is an archetypal example of this type of compound.[4]

As a part of our current interest in the chemotaxonomy and pharmacology of the spurge family, we have investigated the secondary metabolites of *Euphorbia terracina* L.[5] The isolation and structure elucidation of seven δ lactones, terracinolides A−G, characterized by a novel bishomoditerpene (C_{22}) carbon framework, have been described in two recent papers.[6,7] More recently, we reported the isolation of 11 new polyoxygenated jatrophane derivatives, as well as of a rearranged jatrophane displaying a novel carbon framework.[8] In the present paper, we complete the chemical study of this species with the description of **1** and five further C_{22} lactones, four of which (**2**, **3**, **5**, **6**) are new. Two of these have an eight-membered lactone ring as a novel structural feature and have been named isoterracinolides A (**5**) and B (**6**). We further describe a new *ent*-abietanolide (**7**) belonging to the jolkinolide structural type. The structures of all compounds, including stereochemical aspects, have been obtained with the aid of extensive spin decoupling, 2D NMR, and NOE measurements.[9]



1 R = R′= Ac
2 R = Ac R′ = H
3 R = Bz R′ = H



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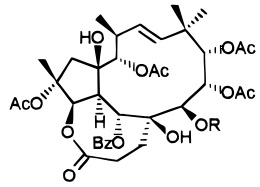
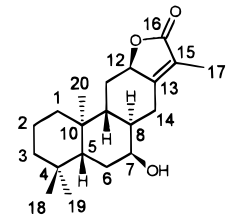


5 R = COiPr
6 R = COEt



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Results and Discussion

Compounds **1**−**4** gave NMR spectra that closely resembled those of the previously reported terracinolides A−G.[6,7] The first described examples of this compound class had no oxygen function at C-13. However, *E. segetalis* was recently reported to contain several terracinolides,[10] two of them being **1** (13α-hydroxy terracinolide B) and **4** (13α-hydroxy terracinolide I). The NMR features of **2** and **3** resemble very closely those of **1**. The only difference between **1** and **2** is the absence in the latter of one of the acetyl groups present in the former. The strong similarity between the ^{1}H NMR spectra of both compounds and the characteristic differences in the ^{13}C NMR chemical shifts of the carbon atoms around C-15 (C-1 and C-14 shifted downfield and C-15 shifted upfield) indicated that **2** is the 15-*O*-deacetyl derivative of **1**. The acylation pattern of **2** corresponds, therefore, to that of terracinolide G[7] with addition of a hydroxyl group at C-13α. Consequently, compound **2** has been named 13α-hydroxy terracinolide G. In the same way, the spectral features of compound **3** clearly correspond to those of **2** with the mere replacement of the 6-acetoxy by a 6-benzoyloxy group. This conclusion was particularly supported by the absence of HMBC correlations between the benzoyl carbonyl group and the ring protons, as well as by the NOEs observed between the ortho benzene protons and H-5/H-8/H-12. The resulting acylation pattern corresponds to that of terracinolide A[6] with addition of a 13α-OH group and deacetylation at C-15. Lactone **3** is thus 15-*O*-deacetyl 13α-hydroxy terracinolide A. The absolute configuration of these bishomojatrophane lactones has not been determined and has been assumed to be the same as in other structurally similar, naturally occurring jatrophane derivatives.[11] The main conformation of **2** was calculated by PCMODEL.[12]

Although the NMR features of **5** and **6** (Table 1 and Experimental Section) are similar to those of the terraci-

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Table 1. ^{1}H NMR Data of Lactones **2**, **3**, **5**, and **6**[a]

H	**2**[b]	**3**[c]	**5**[d]	**6**[e]
1α	3.69 d (16.5)	3.61 d (16.5)	2.82 d (16.5)	2.82 d (16.5)
1β	1.94 d (16.5)	1.85 d (16.5)	2.22 d (16.5)	2.22 d (16.5)
3	5.47 d (4.5)	5.54 d (4.5)	5.46 d (4)	5.48 d (3.5)
4	3.77 dd (10, 4.5)	3.89 dd (10.5, 4.5)	2.97 dd (4, 3.5)	2.97 t (3.5)
5	5.30 d (10)	5.64 d (10.5)	6.56 d (3.5)	6.57 d (3.5)
7	5.89 s	6.03 s	5.32 s	5.30 s
8	5.45 s	5.70 s	5.69 d (6)	5.69 d (6)
9	4.90 s	5.01 s	4.95 d (6)	4.95 d (6)
11	6.16 br d (16.5)	6.19 br d (16.5)	5.49 d (16)	5.49 d (16)
12	5.71 d (16.5)	5.80 d (16.5)	5.76 dd (16; 10)	5.77 dd (16, 10)
13			2.66 m	2.67 dq (10; 7)
14			5.02 s	5.03 s
16	1.53 s	1.50 s	1.73 s	1.73 s
17α	2.40 m	2.70 m	1.68 ddd (14; 7; 2)	1.69 ddd (14; 7; 2.5)
17β	1.90 m	2.00 m	1.82 ddd (14; 14, 3)	1.83 ddd (14; 14; 2.5)
18	0.96 s	1.00 s	0.96 s	0.96 s
19	1.26 s	1.45 s	1.03 s	1.03 s
20	1.56 s	1.45 s	1.08 d (7)	1.09 d (7)
21α	2.40 m	2.51 br dd (15; 4)	3.17 ddd (14; 14; 2)	3.20 ddd (14; 14; 2.5)
21β	3.29 ddd (15, 15, 6.5)	3.53 ddd (15; 15; 6)	2.30 ddd (14; 7; 3)	2.32 ddd (14; 7; 2.5)
OAc	2.16 s, 2.07 s, 2.05 s, 2.01 s, 2.00 s	2.13 s, 2.08 s, 2.07 s, 2.00 s	2.35 s, 2.18 s, 2.15 s, 2.12 s	2.35 s, 2.19 s, 2.15 s, 2.13 s
^{i}PrCO	2.63 sept (7)	2.70 sept (7)	2.66 sept (7)	
	1.27 d (7), 1.23 d (7)	1.31 d (7), 1.23 d (7)	1.19 d (7), 1.18 d (7)	

[a] ^{1}H Chemical shifts (ppm) are followed by coupling constants (Hz) in parentheses. [b] OH groups: 13-OH, 3.95 s; 15-OH, 4.20 s. [c] OH groups: 13-OH, 4.10 s s; 15-OH, 4.05 s; benzoate group: 7.85 dd (8.5, 1.5), 7.65 tt (8.5, 1.5), 7.50 dt (8.5, 1.5). [d] OH groups: 6-OH, 3.50 br s, 15-OH, 2.40 s; benzoate group: 8.06 dd (8, 2), 7.55 tt (8, 2), 7.44 dt (8, 2). [e] OH groups: 6-OH, 3.55 s, 15-OH, 2.40 s; benzoate group: 8.06 dd (8, 2), 7.55 tt (8, 2), 7.44 dt (8, 2); propionate group: 2.44 q (2H, 7.5), 1.14 t (3H, 7.5).

nolides, some differences deserve comment. Lactone **5** was assigned the molecular formula $C_{41}H_{54}O_{16}$ (M = 802) on the basis of ^{13}C NMR data, which indicated the presence of six ester groups: four acetates, one isobutyrate, and one benzoate. The highest peak in the MS (*m/z* 784) appeared 18 amu below the expected value, a fact explained by the loss of water from the parent peak. In contrast with the previously described C_{22} lactones, no ketone carbonyl group was present, but an additional acylated secondary alcohol appeared instead. Other features of the terracinolide structure (one lactone carbonyl, one *trans* disubstituted C=C bond, one gem-dimethyl group, etc.) were also present. Extensive spin decoupling and 2D experiments revealed the same carbon−hydrogen connectivities present in the terracinolides with some differences. For instance, the three-hydrogen chain H7−H8−H9 appeared no longer as three singlets but as a singlet (H-7) and two doublets (J = 6 Hz). Likewise, the H3−H4−H5 segment displayed J values quite different from those of the other terracinolides. The clue to the structure came from a careful examination of the HMBC correlations, most particularly those of the ester carbonyls with their geminal hydrogen atoms ($^3J_{C-H}$ in the fragment O=C−O−C−H).[7,13] With the aid of these correlations, three acetoxy groups were located at C-8, C-9, and C-14; the isobutyrate group was ascribed to C-7, and the benzoate group was situated at C-5. In consequence, the δ lactone ring of the terracinolides was not present here. Two free OH groups were located at C-6 and C-15 on the basis on HMBC correlations (15-OH with the neighbor carbons) and NOE measurements (6-OH with H-5 and with the benzene ortho protons). The fourth acetoxy group was clearly at C-2, in view of the NOE of its hydrogens with H-16. The only remaining possibility was the formation of an eight-membered lactone ring between the carboxyl chain at C-6 and the C-3 hydroxyl group. This conclusion was supported by a quite weak, but still visible, correlation between the lactone carbonyl and H-3. Further support came from the NOEs observed between H-4 and H-5 with H-8. This observation is not compatible with the δ lactone structure of the terracinolides but is easily explained with the structure depicted. In the main conformation of **5**, as calculated by PCMODEL,[12] the aforementioned hydrogen pairs are quite close (<2.5 Å). We thus propose structure **5** for the compound under study, which we name isoterracinolide A.

The NMR spectral features of compound **6** (Table 1 and Experimental Section) were very close to those of **5**. The only difference was that **6** contained a propionate group instead of an isobutyrate. Examination of HMBC correlations and NOE data revealed that the structure of **6** corresponds to that of **5** with substitution of the aforementioned acyl groups at C-7. Lactone **6** was thus named isoterracinolide B.

The structure of compound **7** differred from those of the other lactones found in the plant according to its NMR spectra (Experimental Section). IR, MS, and ^{13}C NMR data of **7** indicated the molecular formula $C_{20}H_{30}O_3$, the presence of a secondary hydroxyl group and a conjugated γ lactone, and a tetrasubstituted C=C bond. The compound was therefore carbotricyclic, with an additional ring from the lactone moiety. The ^{1}H NMR spectrum pointed out the presence of three methyl singlets and one olefinic methyl. These data indicated an abietane lactone of the jolkinolide/helioscopinolide type.[14] Extensive spin decoupling and 2D HMQC/HMBC experiments confirmed this hypothesis, which was also supported by comparison with literature data.[14] NOE measurements together with J values allowed assignment of configurations to the key stereogenic centers. Compound **7** is structurally close to jolkinolide E (= helioscopinolide G)[14] and has thus been named 7β-hydroxy-8α,14-dihydro jolkinolide E.

Some jatrophane derivatives isolated from *E. terracina* have been shown to display a pharmacological action on vascular tissues, as well as weak antitumor activity.[9,15] None of the compounds found in the plant, however, exhibits the irritant action found in other typical diterpenes[1−4] from the family Euphorbiaceae.

Experimental Section

General Experimental Procedures. 1D and 2D NMR spectra were measured at 22 °C in a Varian Unity spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) equipped with an inverse probehead. Standard Varian software was used for these measurements. The signals of the deuterated solvent ($CDCl_3$) were obtained as the reference (the singlet at 7.25 for ^{1}H NMR and the triplet centered at 77.00 ppm for ^{13}C NMR data). MS were run in the electron impact (EI) mode (70 eV). In one case, the FAB mode was used for the detection of the parent peak. Samples for IR spectral measurements were prepared as KBr pellets (solids) or as films on NaCl plates (oils). Melting points are not corrected. Column chromatography was performed on Si gel Süd-Chemie (60−200 μm). Si gel RP-2 was from Merck (Art. 07719). Preparative HPLC was performed in the reversed-phase mode with a LiChrosorb RP-8 column (detection by refraction index), using MeOH−H_2O or MeCN−H_2O mixtures. The H_2O content varied within the range 25−45%, according to the polarity of the sample on normal Si gel (more polar samples required a higher H_2O content for a good separation).

Plant Material. *Euphorbia terracina* was collected in the shore near El Saler (Valencia, Spain) in June 1992. A voucher specimen (BCF-37210) has been deposited in the Herbarium of the Laboratory of Botany, Faculty of Pharmacy, University of Barcelona, Spain (Prof. J. Vallés-Xirau).

Extraction and Isolation. *E. terracina* (whole aerial parts, 680 g) was air-dried, ground, and extracted at room temperature with MeOH−H_2O 9:1. The extract was concentrated in vacuo, weighed, and dissolved in the minimum amount of boiling MeOH. After adding Si gel RP-2 to the solution (3 g Si gel/1 g extract), the solvent was totally eliminated in vacuo. The greenish, powdery material was then placed on the top of a glass chromatographic column filled with Si gel RP-2. Elution was performed first with H_2O, then with MeOH−H_2O 70:30, and finally with MeOH. Only the middle fraction was investigated further, as the other two were shown to contain only sugars and highly polar compounds (H_2O fraction) and waxes, sterols, and similar compounds of low polarity (MeOH fraction).

The MeOH−H_2O fraction was separated into three main fractions by chromatography on Si gel with hexane−Et_2O 1:1, Et_2O, and Et_2O−MeOH 6:1. The Et_2O fraction was subjected to Si gel chromatography with hexane−Et_2O mixtures of increasing polarity. The intermediate fractions were further purified using HPLC. This allowed the isolation (in order of increasing polarity on Si gel), of **7** (5 mg), **5** (14 mg), **6** (6 mg), **1** (32 mg), **3** (36 mg), **4** (13 mg), and **2** (24 mg).

13α-Hydroxy terracinolide B (1): oil; $[\alpha]^{24}_D$ +12.5° (*c* 4, $CHCl_3$); IR (KBr) ν_{max} 3450 (br), 1765, 1744, 1728, 1713 cm^{-1}; ^{1}H and ^{13}C NMR, see Yuste;[9] EIMS *m/z* 796 $[M]^+$ (1), 768 $[M - CO]^+$ (5), 708 $[M - CO - HOAc]^+$ (47), 666 $[M - CO - HOAc - ketene]^+$ (16), 648 (14), 606 (24), 546 (18), 518 (26), 458 (23), 398 (8), 192 (100), 112 (51), 71 (68); HREIMS *m/z* 796.3127 (calcd for $C_{38}H_{52}O_{18}$, 796.3153).

13α-Hydroxy terracinolide G (2): oil; $[\alpha]^{24}_D$ +19.5° (*c* 2.4, $CHCl_3$); IR (KBr) ν_{max} 3450 (br), 1767, 1758, 1752, 1748, 1728, 1713 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 214.7 (C-14), 176.0 (isobutyrate C=O), 172.3 (C-22), 170.4, 169.8, 169.7, 169.4, 168.8 (acetate C=O), 132.1 (C-11 + C-12), 87.1 (C-2), 85.1 (C-15), 82.6 (C-13), 81.8 (C-3 + C-6), 80.8 (C-9), 72.6 (C-5), 68.2 (C-7), 67.5 (C-8), 50.7 (C-1), 45.7 (C-4), 39.5 (C-10), 34.5 (isobutyrate CH), 30.3 (C-20), 28.7 (C-21), 25.9 (C-18), 25.7 (C-17), 22.2 (C-19 + acetate Me), 22.3, 21.0, 20.7, 20.6 (acetate Me), 19.5 (C-16), 18.9, 18.2 (isobutyrate Me); EIMS *m/z* 694 $[M - HOAc]^+$ (6), 666 $[M - CO - HOAc]^+$ (8), 634 (16), 606 (11), 518 (35), 458 (14), 112 (60), 71 (100); HREIMS *m/z* 694.2880 (calcd for $C_{34}H_{46}O_{15}$, 694.2837); HRFABMS *m/z* 755.3115 $[M + H]^+$ (calcd for $C_{36}H_{51}O_{17}$, 755.3126).

15-O-Deacetyl-13α-hydroxy terracinolide A (3): oil; $[\alpha]^{24}_D$ +31.5° (*c* 2.7, $CHCl_3$); IR (KBr) ν_{max} 3450 (br), 1767, 1755, 1744, 1732 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.8 (C-14), 176.4 (isobutyrate C=O), 172.4 (C-22), 170.6, 169.8, 169.7, 169.5 (acetate C=O), 165.4 (benzoate C=O), 133.7, 130.2, 129.5, 128.4 (aromatic), 132.5 (C-11), 131.6 (C-12), 87.1 (C-2), 85.0 (C-15), 82.4 (C-13), 82.2 (C-3), 81.8 (C-6), 81.5 (C-9), 73.1 (C-5), 69.6 (C-7), 68.0 (C-8), 50.9 (C-1), 46.4 (C-4), 39.9 (C-10), 34.6 (isobutyrate CH), 30.4 (C-20), 29.1 (C-21), 27.0 (C-17), 25.8 (br, C-18), 23.0 (br, C-19), 22.4, 21.1, 20.8, 20.7 (acetate Me), 19.6 (C-16), 18.9, 18.1 (isobutyrate Me); EIMS *m/z* 816 $[M]^+$ (1), 788 $[M - CO]^+$ (1), 770 $[M - CO - H_2O]^+$ (1), 696 $[M - 2HOAc]^+$ (3), 668 (7), 580 (28), 458 (12), 398 (5), 105 (100), 71 (21); HREIMS *m/z* 816.3241 (calcd for $C_{41}H_{52}O_{17}$, 816.3204).

13α-Hydroxy terracinolide I (4): white needles (hexane−EtOAc), mp 240−242 °C; $[\alpha]^{24}_D$ +44.3° (*c* 9.2, $CHCl_3$); IR (KBr) ν_{max} 3450 (br), 1763, 1744, 1728, 1709 cm^{-1}; ^{1}H and ^{13}C NMR, see Yuste;[9] EIMS *m/z* 812 $[M]^+$ (3), 710 $[M - HOAc - ketene]^+$ (2), 664 $[M - HOAc - {}^i PrCOOH]^+$ (17), 622 (37), 553 (32), 261 (41), 123 (100), 112 (81), 71 (75); HREIMS *m/z* 812.3079 (calcd for $C_{38}H_{52}O_{19}$, 812.3102).

Isoterracinolide A (5): oil; $[\alpha]^{24}_D$ +3.7° (*c*, 2.1, $CHCl_3$); IR (KBr) ν_{max} 3450 (br), 1770, 1760, 1745, 1730 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.6 (isobutyrate C=O), 173.4 (C-22), 171.9, 171.2, 170.1, 169.6 (acetate C=O), 168.0 (benzoate C=O), 133.9, 130.1, 128.8, 128.6 (aromatic), 134.8 (C-11), 133.9 (C-12), 88.8 (C-2), 85.4 (C-15), 84.8 (C-3), 81.9 (C-6), 80.4 (C-14), 78.2 (C-9), 77.8 (C-5), 70.1 (C-8), 67.8 (C-7), 51.9 (C-1), 44.2 (C-4), 40.8 (C-10), 37.0 (C-13), 34.0 (isobutyrate CH), 31.7 (C-17), 28.0 (C-21), 26.5 (C-18), 22.9, 21.6, 21.4, 20.8 (acetate Me), 22.4 (C-20), 20.9 (C-19), 19.8 (C-16), 19.0, 18.5 (isobutyrate Me); EIMS *m/z* 784 $[M - H_2O]^+$ (2), 742 $[M - HOAc]^+$ (1), 725 (10), 682 (3), 671 (7), 620 (10), 573 (24), 105 (100), 71 (26); HREIMS *m/z* 784.3285 (calcd for $C_{41}H_{52}O_{15}$, 784.3306).

Isoterracinolide B (6): oil; $[\alpha]^{24}_D$ −20.5° (*c*, 0.5, $CHCl_3$); IR (KBr) ν_{max} 3450 (br), 1745, 1740, 1730 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.4 (propionate C=O), 173.5 (C-22), 171.9, 171.2, 170.3, 169.6 (acetate C=O), 168.2 (benzoate C=O), 134.0, 130.1, 128.8, 128.6 (aromatic), 134.7 (C-11), 133.9 (C-12), 88.8 (C-2), 85.4 (C-15), 84.7 (C-3), 81.8 (C-6), 80.4 (C-14), 78.3 (C-9), 77.8 (C-5), 70.1 (C-8), 68.1 (C-7), 51.9 (C-1), 44.2 (C-4), 40.7 (C-10), 36.9 (C-13), 31.9 (C-17), 28.1 (C-21), 27.3 (propionate CH_2), 26.4 (C-18), 22.9, 21.7, 21.4, 20.8 (acetate Me), 22.4 (C-20), 20.9 (C-19), 19.8 (C-16), 8.7 (propionate Me); EIMS *m/z* 770 $[M - H_2O]^+$ (1), 710 $[M - H_2O - HOAc]^+$ (1), 650 $[M - H_2O - 2HOAc]^+$ (4), 446 (8), 352 (11), 105 (100); HREIMS *m/z* 770.3123 (calcd for $C_{40}H_{50}O_{15}$, 770.3149).

7β-Hydroxy-8α,14-dihydro jolkinolide E (7): oil; $[\alpha]^{24}_D$ −105.5° (*c* 1.25, $CHCl_3$); UV (MeOH) λ_{max} 221, 325 nm; IR (KBr) ν_{max} 3450 (br), 1728, 1686 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.80 (1H, ddq, *J* = 8.5, 8.2, 1.5 Hz, H-12), 3.98 (1H, ddd, *J* = 3, 3, 2.5 Hz, H-7), 2.80 (1H, br dd, *J* = 19, 11.5 Hz, H-14β), 2.50 (1H, ddq, *J* = 19, 5.8, 1.5 Hz, H-14α), 2.16 (1H, ddd, *J* = 13.5, 8.2, 5.8 Hz, H-11α), 1.94 (1H, dddd, *J* = 13, 11.5, 5.8, 3 Hz, H-8), 1.78 (3H, ddd, *J* = 1.5, 1.5, 1.5 Hz, H-17), 1.75 (1H, ddd, *J* = 14, 4, 3 Hz, H-6β), 1.65−1.55 (2H, m, H-1α, H-6α), 1.55−1.50 (2H, m, H-2α, H-9), 1.50−1.40 (2H, m, H-2β, H-3α), 1.34 (1H, dd, *J* = 13.5, 4 Hz, H-5), 1.30−1.25 (1H, m, H-11β), 1.18 (1H, ddd, *J* = 13, 13, 4 Hz, H-3β), 0.89 (3H, s, H-20), 0.88 (1H, m, H-1β), 0.84 (3H, s, H-18), 0.82 (3H, s, H-19); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.4 (C-16), 163.4 (C-13), 120.5 (C-15), 78.5 (C-12), 68.9 (C-7), 46.8 (C-5), 42.5 (C-9), 42.0 (C-3), 38.0 (C-1 + C-10), 35.1 (C-8), 33.1 (C-18), 32.7 (C-4), 30.2 (C-6), 27.5 (C-11), 26.7 (C-14), 21.6 (C-19), 18.4 (C-2), 12.6 (C-20), 8.4 (C-17); EIMS *m/z* 318 $[M]^+$ (97), 300 $[M - H_2O]^+$ (97), 285 $[M - H_2O - Me]^+$ (78), 272 (33), 257 (12), 229 (14), 215 (25), 203 (17), 189 (20), 177 (52), 164 (66), 137 (100), 123 (56), 109 (33), 91 (26), 81 (32), 69 (41), 55 (35); HREIMS *m/z* 318.2193 (calcd for $C_{20}H_{30}O_3$, 318.2194).

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