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Synthesis of (+)-6β−Isovaleryloxylabda-8,13-diene-7α,15-diol, a Metabolite from *Trismusculus reticulatus*

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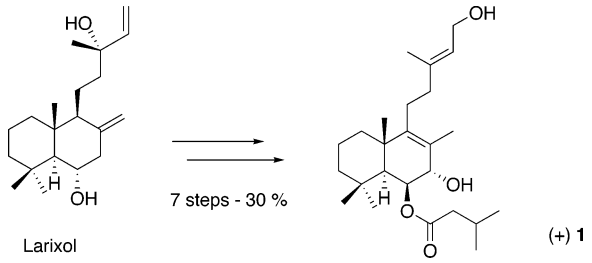


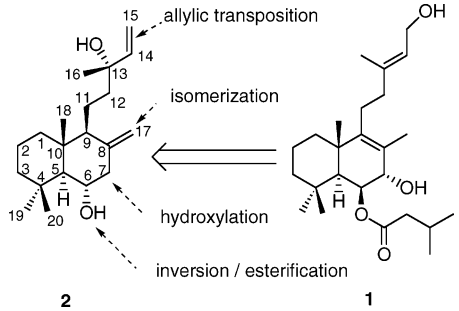
A seven-step synthesis of (+)-6β-isovaleryloxylabda-8,13-diene-7α,15-diol has been achieved starting from (+)-larixol; this allowed determination of the absolute configuration of the metabolite isolated from the mucus of *Trimusculus reticulatus*.

Unlike most intertidal limpets, *Trimusculus reticulatus* filter feeds by producing a mucus net which traps phytoplankton;[1] the mucus is also produced when this sessile marine organism is disturbed. Since *T. reticulatus* is prey of few predators and as the mucus has been shown to repell starfish,[2] the role of its secondary metabolites as protective agents in it has been put forward. 6β-Isovaleryloxy-labda-8,13-diene-7α,15-diol (**1**) was isolated from the mucus;[3] since **1** is highly toxic[1] to larvae of *Phragmatopoma california*, a putative intertidal competitor worm, it is a likely candidate to be active in defense mechanisms of *T. reticulatus.*

A 18-step synthesis of **1** (22% overall yield), under racemic form, has been reported;[4] in this work, a shorter synthesis of **1**, and under optically active form so as to determine its absolute configuration, is presented.

Toward this goal (+)-larixol (**2**) was selected as a suitable starting material because of its attractively functionalized *trans*-decaline ring system. In addition, larixol is easily extracted from the oleoresin of larch tree in which it is abundant.[5] The potential of larixol in synthesis has been demonstrated by the preparation of

SCHEME 1. Retrosynthetic Analysis



terpenoids such as borjatriol,[6] uvidin-C,[7] 6-oxo-ambrox,[8] hedychenone, and yunnancoronarins A and D.[9] The retrosynthetic analysis for **1** is outlined in Scheme 1.

The synthesis commenced with isomerization of the exocyclic double bond of **2**; when larixol was treated with *N*-lithioethylenediamine[10,11] a mixture of isomers **3** and **4** was obtained;[12] as these diols can be separated by column chromatography with difficulty it is advisable to oxidize the crude reaction mixture (Scheme 2), separation of ketones **5** and **6** being much easier. For the allylic oxidation at C-7 of **5**, Cr(VI)-based oxidations were considered but conditions avoiding that of the allylic hydroxyl group on the side chain[13] and/or isomerization to a conjugated enone are required. With PDC in the presence of *tert*-butyl hydroperoxide (3 equiv each)[14] although there was no evidence for formation of the desired allylic alcohol, structure **7** was assigned to one component which was, however, formed in a nonreproducible and low yield. For selenium dioxide-based oxidations, some reaction occurred in dioxane when water was present, but this was slow as after overnight treatment 60% of **5** remained unreacted. Nevertheless, the mixture contained two oxidized compounds which were best separated from each other after reductive treatment; diol **8**[15] and a triol were isolated. Molecular modeling (Insight II) of the triol (performed with both configurations at C-7) resulted in predicted values of $J_{6\alpha,7\alpha} = 2$ Hz and $J_{6\alpha,7\beta} = 6$ Hz; since both H-6 and H-7 signals are experimentally observed to be broad singlets (*i.e.*, vicinal couplings $J_{5,6}$ and $J_{6,7}$ are small), structure **9** was assigned. Selective protection of the more reactive secondary allylic hydroxyl group as a silyl ether (to get **10**) and introduction of the

(1) Manker, D. C.; Faulkner, J. *J. Chem. Ecol.* **1996**, *22*, 23−35.
(2) Rice, S. H. *Exp. Mar. Biol. Ecol.* **1985**, *93*, 83−89.
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(4) Gao, W.-G.; Sakaguchi, K.; Isoe, S.; Ohfune, Y. *Tetrahedron Lett.* **1996**, *37*, 7071−7074.
(5) Larixol is present (up to 10−20% w/w) in the oleoresin of several larch species; see: Mills, J. S. P*hytochemistry* **1973**, *12*, 2407−2412.
(6) Herlem, D.; Khuong-Huu, F. *Tetrahedron* **1997**, *53*, 673−680.
(7) Lagnel, B. M. F.; Morin, C.; de Groot, A. *Synthesis* **2000**, 1907−1916.
(8) Bolster, M. G.; Lagnel, B. M. F.; Jansen, B. J. M.; Morin, C.; de Groot, A. *Tetrahedron* **2001**, *57*, 8369−8379.
(9) Aslaoui, J.; Li, H.; Morin, C. *Tetrahedron Lett.* **2005**, *46*, 1713−1716.
(10) Reggel, L.; Friedman, S.; Wender, I. *J. Org. Chem*. **1958**, *23*, 1136−1139.
(11) Caputo, R.; Mangoni, L.; Monaco, P.; Previtera, L. *Phytochemistry* **1974**, *13*, 471−474.
(12) We found the proportion of **3** and **4** to vary with reaction conditions (from 3:2 to 4:1), but these could be adjusted (see the Experimental Section) so that the desired compound **3** was preponderant and formed in a reproducible way.
(13) Morin, C.; Nedjar, N. *Tetrahedron Lett*. **1996**, *37*, 4705−4706.
(14) (a) Chidambaram, N.; Chandrasekaran, S. *J. Org. Chem*, **1987**, *52*, 5048−5051. (b) Levin, J. I. *Tetrahedron Lett.* **1996**, *37*, 3079−3082.
(15) No efforts were undertaken to assign the stereochemistry at C-9 of **8**.

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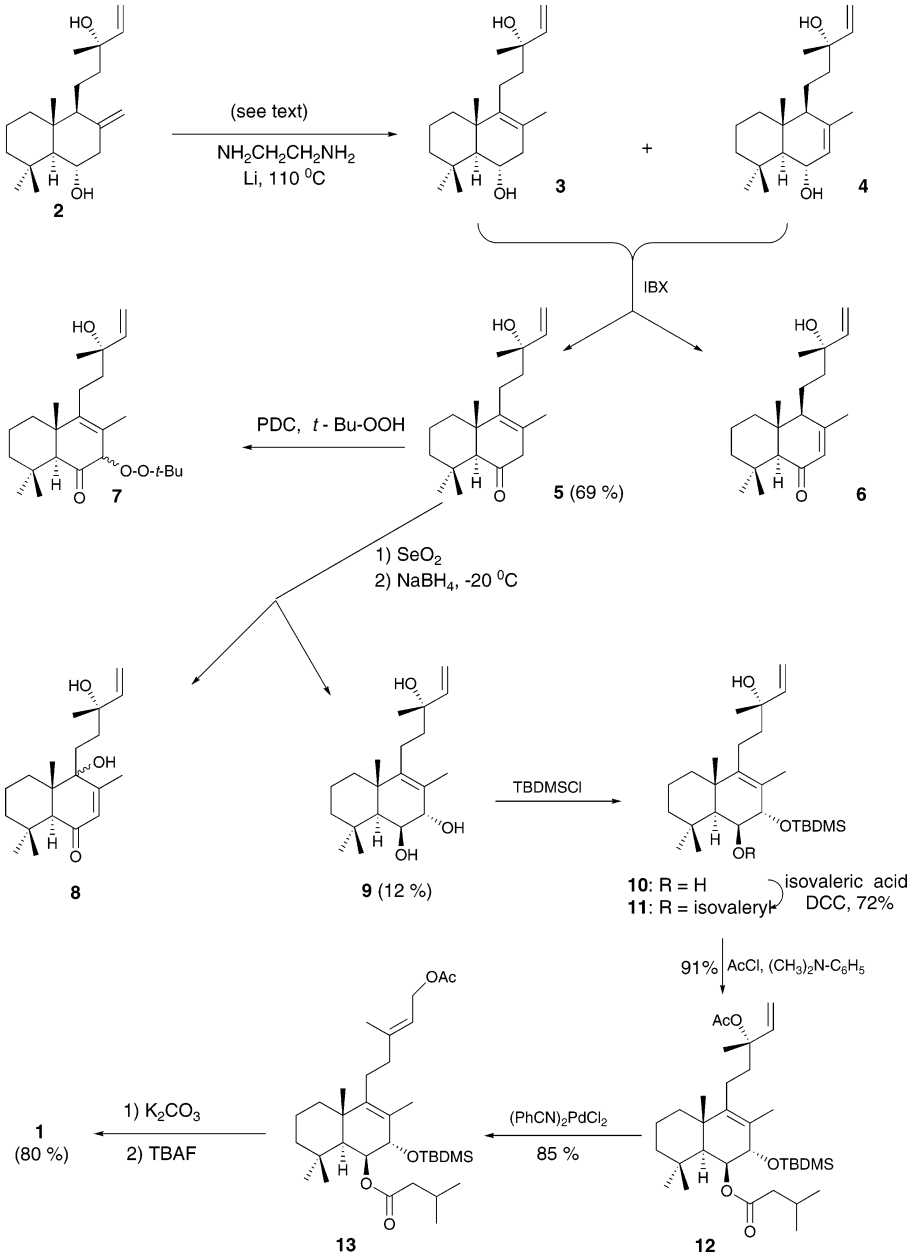
SCHEME 2



isovaleryl unit at O-6 by a DCC-mediated esterification afforded **11**. Acetylation of the tertiary hydroxyl group could be accomplished in the presence of *N*,*N*-dimethylaniline,[16] and **12** thus obtained was subjected to a Pd(II)-catalyzed rearrangement;[17] this proceeded smoothly and afforded **13** in a stereoselective manner;[18] after two sequential deprotection steps the desired compound **1** was obtained. Although this scheme was "satisfactory" in that it delivered **1**, the overall yield was poor and a better route was therefore explored.

To shorten the synthesis, introduction of the 6-isovaleryloxy group before allylic oxidation was considered as this would avoid a protection/deprotection sequence at O-7; the allylic rearrangement was also planned using a 13-isovaleryloxy group so as to further reduce the number of steps (Scheme 3). Thus, **5**, readily obtained from larixol by isomerization and then oxidation with IBX[19] (Scheme 2), was reduced to afford **14** (the epimer of **3**). This diol **14** was bis-esterified (to get **15**) and SeO_2 oxidation of **15** then cleanly delivered **16**.[20] The remaining steps benefited from results obtained with **12** as allylic rearrangement[18] and selective saponification of the allylic

(16) (a) Ohloff, G. *Helv. Chim. Acta* **1958**, *41*, 845−850. (b) Sandermann, W.; Bruns, K. *Chem. Ber.* **1966**, *99*, 2835−2841. (c) Bol'shakova, V. I.; Shmidt, E. N.; Pentegova, V. A.; Mamatyuk, V. I. *Khim. Prir. Soedin*. **1986**, 571−6 (Engl. Transl. 536−540).

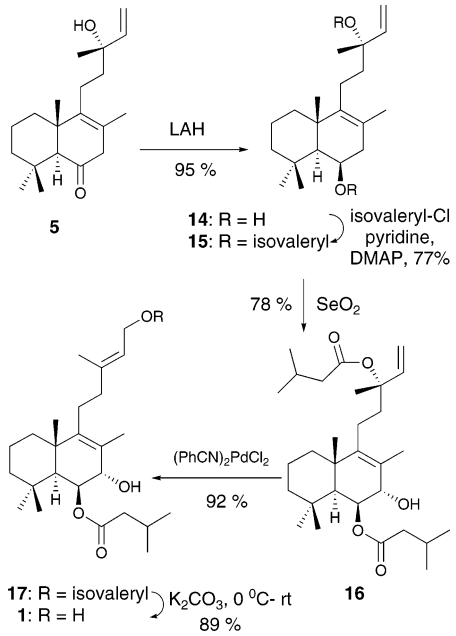
(17) Overman, L. E.; Knoll, F. M. *Tetrahedron Lett.* **1979**, 321−324.

(18) No *Z* isomer was detected in the NMR of the crude reaction mixture, and there is literature precedent for such stereoselectivity in this rearrangement; for labdane derivatives, see ref 8 and: Zahra, J.-P.; Chauvet, F.; Coste-Maniere, I.; Martres, P.; Perfetti, P.; Waegell, B. *Bull. Soc. Chim. Fr.* **1997**, *131*, 1001−1024. For another example, see: Grieco, P. A.; Tagikawa, T.; Bongers, S. L.; Tanaka, H. *J. Am. Chem. Soc.* **1980**, *102*, 7588−7590.

(19) More J. D.; Finney, N. S. *Org. Lett.* **2002**, *4*, 3001−3003.

(20) As in the case of **9**, both H-6 and H-7 NMR-signals are broad singlets.

SCHEME 3



ester of **17** thus obtained afforded (+)-**1** (>30% overall yield from larixol).

The spectral data of (+)-**1** were compared to those reported for the natural product,[3] and they fully matched.[21] The *E*-configuration of the side-chain double bond was established by a NOESY experiment which showed a correlation between H-15 and CH_3-16. Since the optical rotation of **1** is in accordance with that of the natural product[3] and as the absolute configuration of larixol from which (+)-**1** has been synthesized is known,[22] the absolute configuration of (+)-**1** is firmly established.

Experimental Section

All reagents and solvents were purchased from standard sources except for IBX which was prepared according to ref 23. NMR spectra are referenced from the residual absorption of C*H*Cl_3 (δ = 7.26 ppm) and *C*DCl_3 (δ = 77.0 ppm); ^{13}C NMR assignments have been made by comparison with those of manool[24] and DEPT experiments.

13(*S*)-Hydroxylabda-8, 14-dien-6-one (5). Ethylenediamine (235 mL, 3.5 mol) was added with stirring to lithium wire (3.38 g, 487 mmol) placed under argon, and after 30 min the color of reaction mixture changed to blue; stirring was continued until it became white, at which time larixol (**2**) (6.0 g, 19.6 mmol) was added; the resulting reaction mixture was stirred overnight at 110 °C, and after cooling it was quenched with water and extracted with diethyl ether. The pooled organic layers were washed with water and dried on anhydrous sodium sulfate. After filtration and evaporation of the volatiles, the crude product (mixture of **3** and **4**, 6.3 g) was dissolved in ethyl acetate (150 mL), and IBX (16.3 g, 65.5 mmol) was added. The reaction mixture was refluxed overnight and then cooled to room temperature and filtered through Celite. The Celite was washed with ethyl acetate and the filtrate concentrated under reduced pressure; chromatography of the crude product over silica gel column (95:5, cyclohexane/EtOAc) afforded **5** (4.15 g, 69%) then **6** (1.1 g,; for spectral data, see ref 8). **5**: colorless oil: $[\alpha]^{20}_D$ +160 (*c* 0.53, $CHCl_3$); IR (KBr) 3435, 2930, 2868, 1712, 1698 cm^{-1}; MS (CI with NH_3) *m/z* 322 (M + NH_4)$^+$, 305 (M + H)$^+$, 287 (MH − H_2O)$^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.93 (X part of ABX, 1H, H-14), 5.23 and 5.08 (AB part of ABX, $J_{15,15'}$ = 1 Hz, 1H each, H-15), 2.85 and 2.58 (AB system, $J_{7,7'}$ = 20 Hz, 1H each, H-7), 2.36 (s, 1H, H-5), 2.22 to 0.91 (m), 5 s at 1.61, 1.30, 1.24, 0.97, 0.91 (CH_3-16 to CH_3-20); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 210.3 (C-6), 144.7 (C-14), 141.4, 123.8 (C-8, C-9), 112.0 (C-15), 73.4 (C-13), 63.9 (C-5), 48.4 (C-7), 44.1 (C-10), 42.6, 42.4 (C-3, C-12), 37.0 (C-1), 32.7 (C-18), 32.3 (C-4), 27.7 (C-16), 22.1 (C-11), 21.8, 21.3 (C-17, C-19), 18.65 (C-2), 18.55 (C-20). Anal. Calcd for $C_{20}H_{32}O_2$·0.25H_2O: C, 77.75; H, 10.59. Found: C, 78.01; H, 10.74.

Labda-8,14-diene-6β,13(*S*)-diol (14). Under argon, a solution of **5** (1.0 g, 3.28 mmol) in dry THF (100 mL) was added with stirring to a suspension of LAH (249 mg, 6.5 mmol) in dry THF (100 mL) at 0 °C; after 1 h of stirring, the reaction mixture was carefully quenched with methanol and filtered through Celite. The Celite was washed with THF, and the filtrate was concentrated; the residue obtained was taken up in ethyl acetate and washed successively with 1 N HCl, water, saturated solution of $NaHCO_3$, and brine and dried on sodium sulfate. After filtration, the volatiles were removed under reduced pressure and the crude product was purified by chromatography (85:15, *n*-pentane/EtOAc) to give **14** (950 mg, 95%): $[\alpha]^{20}_D$ +64 (*c* 0.34; $CHCl_3$); IR (KBr) 3444, 2924, 1727, 1641 cm^{-1}; MS (CI with NH_3) *m/z* 324 (M + NH_4)$^+$, 307 (M + H)$^+$, 306 (M)$^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.93 (X part of ABX, 1H, H-14), 5.21 and 5.06 (AB part of ABX, $J_{15,15'}$ = 1 Hz, 1H each, H-15), 4.43 (br s, 1H, H-6), 2.40 to 1.05 (m), 5 s at 1.59, 1.31, 1.29, 1.20, 0.96, (CH_3-16 to CH_3-20); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.9 (C-14), 139.8, 121.8 (C-8, C-9), 111.8 (C-15), 73.5 (C-13), 65.9 (C-6), 54.0 (C-5), 43.9 (C-7), 43.1, 42.3, 40.0 (C-1, C-3, C-12), 38.9, 34.0 (C-4, C-10), 33.6 (C-18), 27.4 (C-16), 23.8, 21.5 (C-19, C-20), 21.9 (C-11), 19.7 (C-17), 19.2 (C-2). Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 77.95; H, 11.19.

6β,13(*S*)-Diisovaleryloxylabda-8, 14-diene (15). At 0 °C, to a stirred solution of **14** (800 mg, 2.6 mmol) in CH_2Cl_2 (12 mL) were added pyridine (2.12 mL, 26.1 mmol), DMAP (637 mg, 5.2 mmol), and then isovaleryl chloride (3.21 mL, 26 mmol) dropwise. After overnight stirring at room temperature, the reaction mixture was quenched with ice/water and extracted with CH_2Cl_2; the combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ and brine and dried on anhydrous sodium sulfate. After filtration and removal of the volatiles, the crude product was purified by chromatography (95:5, *n*-pentane/EtOAc) to afford **15** (960 mg, 77%) as a colorless oil: $[\alpha]^{20}_D$ +6.0 (*c* 0.65, $CHCl_3$); IR (KBr) 2958, 2931, 2870, 1731, 1641 cm^{-1}; MS (CI with NH_3) *m/z* 492 (M + NH_4)$^+$, 373 (MH − $(CH_3)_2$-$CHCH_2COO$)$^+$, 271 (MH − 2$(CH_3)_2CHCH_2COO$)$^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.97 (X part of ABX system, 1H, H-14), 5.49 (d, *J* = 5.5 Hz, 1H, H-6), 5.15 and 5.13 (AB part of ABX, $J_{15,15'}$ = 1 Hz, 1H each, H-15), 2.37 to 0.91 (m), 5 s and 2 d at 1.56, 1.55, 1.28, 0.98, 0.97, 0.96, 0.94, 0.93, 0.91 (CH_3-16 to CH_3-20, −CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.9, 171.9 (2 × C=O), 141.8 (C-14), 139.3, 122.3 (C-8, C-9), 113.1 (C-15), 82.9 (C-13), 67.8 (C-6), 52.8 (C-5), 44.5, 44.2, 43.3 (C-1, C-3, C-12), 40.3, 40.0, 39.7 (C-7, 2 × −*C*H_2CH(CH_3)$_2$), 39.2, 33.9 (C-4, C-10), 33.5 (C-18), 25.7, 25.5 (2 × −CH_2*C*H(CH_3)$_2$), 23.4, 23.2, 22.5, 22.4, 21.1 (C-16, C-19, C-20, 2 × −CH_2CH(*C*H_3)$_2$), 21.6 (C-11), 19.3 (C-17), 19.1 (C-2). Anal. Calcd for $C_{30}H_{50}O_4$: C, 75.90; H, 10.62. Found: C, 75.71; H, 10.75.

6β,13(*S*)-Diisovaleryloxylabda-8,14-dien-7α-ol (16). To a solution of **15** (600 mg, 1.26 mmol) in dioxane (10 mL) was added a solution of SeO_2 (168 mg, 1.51 mmol) (CAUTION: TOXIC) in dioxane (10 mL) with water (0.75 mL); the mixture was heated at 60 °C for 24 h and cooled to room temperature before filtration through Whattman paper filter. The filtrate was diluted with EtOAc, washed with 20% aqueous solution of sodium sulfite,

(21) In the data given for the synthetic material (ref 4), although it is stated that "synthetic **1** was completely identical with the natural product in all respects", H-6 and H-7 are described as a broad singlet and broad doublet, respectively.

(22) (a) Hauser J. *Bull. Soc. Chim. Fr.* **1965**, 2645−2648. (b) Norin, T.; Ohloff, G.; Willham, B. *Tetrahedron Lett*. **1965**, 3523−3528.

(23) Frigerio, M.; Santagostino, M. *Tetrahedron Lett.* **1994**, *35*, 8019−8022.

(24) (a) Buckwalter, B. L.; Burfitt, I. R.; Nagel, A. A.; Wenkert, E.; Naef, F. *Helv. Chim. Acta* **1975**, *58*, 1567−1573. (b) Almqvist, S. O.; Enzell, C. R.; Wehrli, F. W. *Acta Chem. Scand*. **1975**, *B29*, 695−702.

water, and brine, and dried on anhydrous sodium sulfate. After filtration and removal of the volatiles, the crude product was purified by chromatography (90:10, *n*-pentane/EtOAc) to give **16** (330 mg, 78% on the basis of recovered 190 mg of **15**) as a colorless oil: $[\alpha]^{20}_D$ +36 (*c* 0.49, $CHCl_3$); IR (KBr) 3455, 2959, 2931, 2870,1732, 1641 cm^{-1}; MS (CI with NH_3) *m/z* 472 (MH − H_2O)$^+$, 371 (MH − (H_2O + $(CH_3)_2CHCH_2COO$))$^+$, 269 (MH − (2 × $(CH_3)_2CHCH_2COO$) − H_2O))$^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.97 (X part of ABX, 1H, H-14), 5.26 (s, 1H, H-6), 5.15 and 5.13 (AB part of ABX, 1H each, H-15), 3.63 (br s, 1H, H-7), 2.31 to 0.91 (m) 5 s and 2 d at 1.72, 1.56, 1.25, 0.98, 0.96, 0.94, 0.93, 0.91 (CH_3-16 to CH_3-20, 2 × −CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.0, 171.9 (2 × C═O), 145.3 (C-14), 141.7, 124.4 (C-8, C-9), 113.2 (C-15), 82.8 (C-13), 73.2, 72.6 (C-6, C-7), 48.0 (C-5), 44.5, 44.0, 42.9, 39.9, 39.1, (C-1, C-3, C-12, 2 × −*C*H_2CH$(CH_3)_2$), 39.7, 33.5 (C-4, C-10), 33.2 (C-18), 25.7, 25.5 (2 × −CH_2*C*H-$(CH_3)_2$), 23.5, 23.4, 22.45, 22.35, 21.2 (C-16, C-19). Anal. Calcd for $C_{30}H_{50}O_5$: C, 73.43; H, 10.27. Found: C, 73.56; H, 10.19.

6β,13(*S*)-Diisovaleryloxylabda-8,13-dien-7α-ol (17). Under argon, to a solution of **16** (70 mg, 0.14 mmol) in dry THF (3 mL) was added $(PhCN_2)_2PdCl_2$ (10.7 mg, 0.028 mmol), and the mixture was stirred at room temperature for 3 h. After filtration of the catalyst through a small bed of silica gel, the filtrate was concentrated under reduced pressure. Chromatography of the residue using *n*-pentane/EtOAc (93:7) as eluent afforded **17** (65 mg, 92%) as an oil: $[\alpha]^{20}_D$ +29 (*c* 0.49, $CHCl_3$); IR (KBr) 3452, 2959, 2931, 2870,1735, cm^{-1}; MS (CI with NH_3) *m/z* 472 (MH − H_2O)$^+$, 371 (MH − H_2O − $(CH_3)_2CHCH_2COO$)$^+$, 269 (MH − H_2O − 2 × $(CH_3)_2CHCH_2COO$))$^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.36 (t, $J_{14,15}$ = 6 Hz, 1H, H-14), 5.27 (br s, 1H, H-6), 4.59 (d, $J_{14,15}$ = 6 Hz, 2H, H-15), 3.65 (br d, $J_{6,7}$ = 4 Hz, 1H, H-7), 2.29−0.92 (m) 5 s and 2 d at 1.74, 1.26, 0.99, 0.96, 0.93, 0.92 (CH_3-16 to CH_3-20, 2 × −CH(C*H*$_3$)$_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.1, 173.0 (2 × C═O), 145.6, 142.4 (C-9, C-13), 124.3 (C-8), 118.2 (C-14), 73.3, 72.6 (C-6, C-7), 61.0 (C-15), 48.0 (C-5), 44.0, 43.5, 42.9, 39.4, 39.0, (C-1, C-3, C-12, 2 × −*C*H_2CH$(CH_3)_2$), 39.6, 33.5 (C-4, C-10), 33.2 (C-20), 26.8 (C-11) 25.7, 25.5 (2 × −CH_2*C*H$(CH_3)_2$), 23.5, 22.5, 22.4, 21.1, 19.0, 17.5, 16.5 (C-16, C-17, C-18, C-19, 2 × −CH_2CH(*C*H_3)$_2$), 19.0 (C-2), Anal. Calcd for $C_{30}H_{50}O_5$: C, 73.43; H,10.27. Found: C, 73.74; H = 10.44.

6β-Isovaleryloxylabda-8, 13-diene-7α-15-diol (1). To a stirred solution of **17** (155 mg, 0.36 mmol) in methanol (10 mL) at 4 °C was added potassium carbonate (54 mg, 0.39 mmol), and the mixture was stirred at the same temperature for 1 h and then 9 h at room temperature. The reaction mixture was then diluted with diethyl ether (50 mL), washed with saturated aqueous $NaHCO_3$, water, and brine, and dried on anhydrous sodium sulfate. After removal of solvent, the crude product was purified by chromatography (85:15, *n*-pentane/EtOAc) to give **1** (115 mg, 89%) as a colorless oil: $[\alpha]^{20}_D$ +40.7 (*c* 0.83, $CHCl_3$) [lit.[3] $[\alpha]^{20}_D$ +38.7 (*c* 0.83, $CHCl_3$)]; IR (KBr) 3382, 2957, 2926, 2868, 1732, 1698 cm^{-1}; MS (CI with NH_3) *m/z* 406 (M)$^+$, 388 (M − H_2O)$^+$, 287 (M − (H_2O + $(CH_3)_2CHCH_2COO$))$^+$, 269 (M − (2H_2O + $(CH_3)_2CHCH_2COO$))$^+$; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.43 (t, $J_{14,15}$ = 6.8 Hz, 1H, H-14), 5.25 (t, J = 1.4 Hz, 1H, H-6), 4.15 (d, J = 6.9 Hz, 2H, H-15), 3.64 (d, J = 1.5 Hz, 1H, H-7), 2.26 (d, J = 1.4 Hz, 1H, 6-OH), 2.1−0.8 (m with 1.74 (s, 3H, CH_3-17), 1.71 (s, 3H, CH_3-16), 1.56 (d, J = 1.4 Hz, 1H, H-5), 1.26 (s, 3H, CH_3-18), 1.00 (s, 6H, CH_3-19, CH_3-20), 0.93 (d, J = 6.3 Hz, 6H, −CH(C*H*$_3$)$_2$); after D_2O exchange signals at 4.15 and 3.64 ppm sharpen while that at 2.26 ppm disappears; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.1 (C═O), 145.5 (C-9), 140.0 (C-13), 124.3 (C-8), 123.0 (C-14), 73.4 (C-6), 72.5 (C-7), 59.3 (C-15), 47.9 (C-5), 44.0 (−*C*H_2CH$(CH_3)_2$), 42.9 (C-3), 39.5 (C-10), 39.4 (C-1), 39.0 (C-12), 33.4 (C-4) 33.1 (C-20), 26.9 (C-11), 25.5 (−CH_2*C*H$(CH_3)_2$), 23.4 (C-19), 22.4, 22.3 (−CH_2CH(*C*H_3)$_2$), 21.1(C-18), 19.0 (C-2), 17.6 (C-17), 16.4 (C-16). Anal. Calcd for $C_{25}H_{42}O_4$: C, 73.85; H, 10.41. Found: C, 74.06; H, 10.22 (CH_3-16 to CH_3-20).

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of compound **1** and experimental procedures and spectroscopic data for key compounds of Scheme 2. This material is available free of charge via the Internet at http://pubs.acs.org.

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