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CHEMICAL-MICROBIOLOGICAL SYNTHESES OF 6ß-EUDESMANOLIDES: INCUBATION OF 6ß-ACETOXYEUDESMANES BY *CURVULARIA LUNATA*

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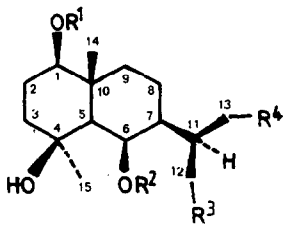
ABSTRACT: Microbial transformation of 6ß-acetoxyeudesmanes by *Curvularia lunata* strain, yielded 12 or 13-hydroxyderivatives as main metabolites. After oxidation with $RuH_2(Ph_3P)_4$, 11-R and 11-S 6ß-eudesmanolides have been obtained.

Eudesmanes sesquiterpenoids have been recently isolated from *Sideritis* genus (Labiatae) in considerable amount [1]. One of these sesquiterpenoids (6ß-acetoxy-1ß,4ß-dihydroxyeudesmane 1) was incubated with *Curvularia lunata* (*C. lunata*) in the course of systematic biotransformations of terpenoids in which we are engaged [2].

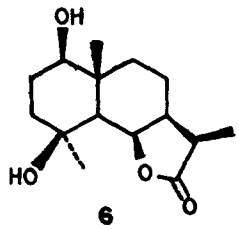


	R^1	R^2	R^3	R^4
1	H	Ac	H	H
2	Ac	Ac	OAc	H
3	Ac	Ac	H	OAc
4	H	H	OH	H
5	H	H	H	OH

In a typical fermentation experiment, substrate 1 was incubated with *C. lunata* (growed in a YEPGA medium, 6 days) for 12 days at 28 °C and 150 r.p.m. in an orbital shaker (250 mg of 1 in 5 mL of EtOH distributed between 10 erlenmeyer flasks). The mycelium was separated by filtration, and the liquid was saturated with NaCl and extracted with CH_2Cl_2 repeatedly. After TLC, a mixture of metabolites was detected, but its separation was problematic. Hence, this mixture was acetylated and flash chromatographed to give two triacetates (2 and 3, 22 and 20 % respectively). These products showed to have an acetoxymethylene group, being epimers at C-11. *C. lunata* hydroxylated the methyl groups of the original isopropyl group of substrate 1.

We have attempted to determine the configuration at C-11 of 2 and 3, but NOE-difference experiments weren't conclusive. However, these remote functionalizations are interesting because they provide a means of obtaining 6ß-eudesmanolides like 6-epiarbusculin and related compounds [3]. Thus, triacetates 2 and 3 were saponified to give 4 and 5 respectively, which were then selectively oxidised with $RuH_2(Ph_3P)_4$ [4] to give directly the

6ß-lactones 6 and 7 without epimerization at C-11. The structure and configuration at C-11 of these lactones have been deduced by mono and bidimensional NMR experiments [5]. Coupling constants for H-11 of lactone 6 (dq, $J_{7,11}$ =



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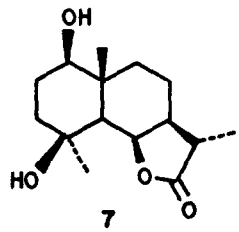

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$J_{11,13}$ = 7.1 Hz) and lactone 7 (q, $J_{11,13}$ = 7.7 Hz) allowed us to assign 11-R configuration for 6 (and 11-S configuration for 7). NOESY experiments also confirmed these configurations, showing dipolar correlation between H-6 and H-11 for the product 6 and between H-6 and H-13, and H-7 and H-13 for the product 7. All considered, we can now assign the configuration at C-11 for the metabolites 2 (11-R) and 3 (11-S).

Lactones 6 and 7 have an equatorial hydroxyl group at C-1, thus, this chemical-microbiological pathway might allow a means of obtaining 6ß-guaianolides (via tosylates), 11,13-dehidroderivatives (via phenylselenide reaction), etc; this being a new procedure to gain access to the scarce sesquiterpenoid 6ß-lactones.

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5.- ^{1}H-NMR of 6 (300 MHz, $CDCl_3$), (δ): 4.74 (1H, dd, $J_{5,6}=J_{6,7}$ = 3.75 Hz, H-6), 2.77 (1H, dq, $J_{7,11}=J_{11,13}$ = 7.1 Hz, H-11), 1.28 (3H, s, 3H-15), 1.20 (3H, d, $J_{11,13}$ = 7.1 Hz, 3H-13), 1.16 (3H, s, 3H-14).

^{1}H-NMR of 7 (300 MHz, $CDCl_3$), (δ): 4.94 (1H, dd, $J_{5,6}$ = 4.7 $J_{6,7}$ = 3.3 Hz, H-6), 2.38 (1H, q, $J_{11,13}$ = 7.7 Hz, H-11), 1.32 (3H, d, $J_{11,13}$ = 7.7 Hz, 3H-13), 1.29 (3H, s, 3H-15), 1.17 (3H, s, 3H-14).

^{13}C-NMR of 6; δ (C): 77.85 (6), 40.55 (11), 178.66 (12), 9.11 (13).

^{13}C-NMR of 7; δ (C): 77.38 (6), 43.44 (11), 179.49 (12), 14.84 (13).

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