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FUNGAL METABOLITES XX (*): CHEMICAL CORRELATION OF LACTARANE AND SECOLACTARANE SESQUITERPENES. ABSOLUTE CONFIGURATION OF FUROSARDONIN A, LACTARAL AND BLENNIN C

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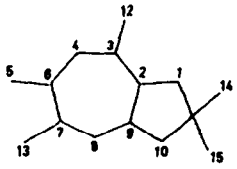
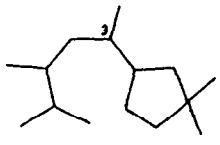
Abstract: The absolute configuration of furosardonin A and secolactarane sesquiterpenes has been established by chemical correlations. Secolactarane lactones and furans have been converted to lactaranes by the Me_2AlCl catalyzed ene reaction.

INTRODUCTION

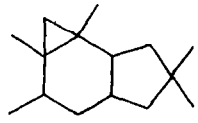
Lactarane and secolactarane sesquiterpenes constitute the largest group of sesquiterpenes isolated so far[1-4] from Russula and Lactarius species (Basidiomycetes) and are believed to derive from marasmane precursors. Indeed velutinal derivatives, possessing the established absolute configurations[3] 1b-c, are considered the only compounds originally present in significant amount in most of these mushrooms and are shown to be transformed to lactarane and secolactarane sesquiterpenes enzymatically[5,6] or chemically.[7]

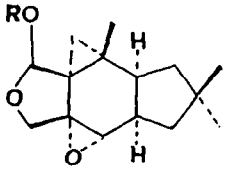


Lactarane



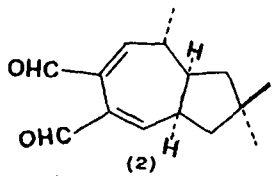
Secolactarane


Marasmane



(1) a R=H
b R=Stearoyl
c R=Oxostearoyl

enzymatic conversion



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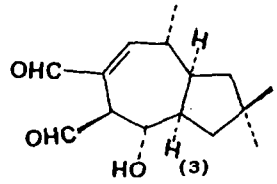
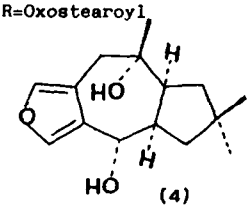


(3)

enzymatic and/or chemical conversion



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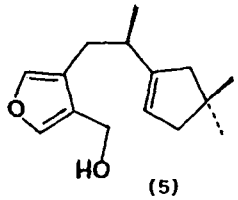
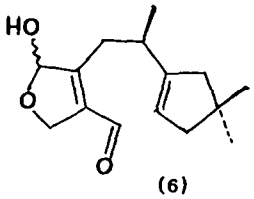


(5)



(6)

However, the dividing line between natural products and possible chemical artifacts is somewhat vague.[1] For example furandiol (4), lactarol (5) and lactardial (6), which can be considered artifacts when formed by chemical degradation of velutinal derivatives, in some ground Lactarius and Russula species also appear to be formed by specific enzymatic routes.[6] Pivotal to these transformations

(*) Part XIX, O. Sterner, R. Bergman, J. Kihlberg, J. Oluwadiya, B. Wickberg, G. Vidari, M. De Bernardi, F. De Marchi, G. Fronza and P. Vita-Finzi, J. Org. Chem. 50, 950 (1985).

of the marasmane skeleton is the breakdown of the fused cyclopropane-cyclohexane bicyclic system with enlargement to a seven membered ring. In this regard interestingly the relative configuration established for the methyl at C-3, with respect to the bridgehead protons H-2 and H-9, can be either cis, as in velleral (2) and piperdial (3), and trans, as in furandiol (4) and other furanoid lactaranes.[7] This stereochemical feature indicates that the crucial cyclopropane ring opening step must occur with at least two different mechanisms and can eventually reflect the different origin of the two sesquiterpenes groups.

The establishment of the stereochemistry of furosardonin A (7), lactaral (8) and the secolactarane 6, then appears of special interest in order to confirm a recently proposed[7] multistep rearrangement of the velutinal skeleton which may mimic the biosynthetic formation of furan and profuran lactaranes. For furosardonin A (7) the trans diaxial relationship existing between the H-8 and H-9 protons is shown by the typical value of the coupling constant (J= 10.5 Hz), whereas the stereochemistry at C-3 has no conclusive evidence.[7]

In this paper we report, for the first time, the conversion of secolactaranes to lactarane sesquiterpenes by the successful application of the ene reaction and the chemical correlation of furosardonin A (7) with compounds having a known stereochemical relationship between H-3 and H-9. In this way the formulas 5-9 have been proved to represent the configuration of these compounds.(*)

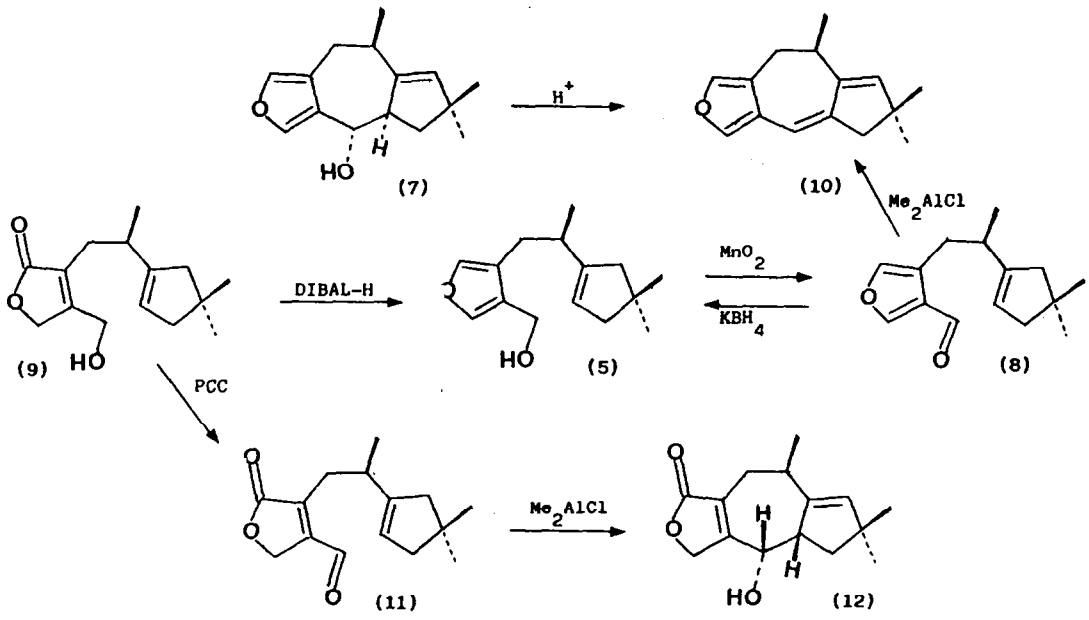
RESULTS AND DISCUSSION

Interconversion of secolactaranes. Beyond secolactaranes of furanoid or profuranoid type, i.e. sesquiterpenes (8) and (6), only one representative of the related class of secolactarane lactones -blennin C[8a] (lactaronecatorin A[8c])- has been isolated so far and its structure assigned[8b] as (9), the stereochemistry at C-3 being undetermined. Blennin C (9) was now reduced with DIBAL-H in THF to the known lactarol (5), which has previously been prepared on KBH_4 reduction[1,9] of both lactaral (8) and lactardial (6). Lactarol, obtained from blennin C, was also oxidized with MnO_2[9] to lactaral (8) having the same rotatory power of a natural sample. Thus all the secolactaranes, both lactones and furans, must have the same absolute configuration.

Conversion of secolactaranes to lactaranes. The oxygen analog of the Lewis acid catalyzed ene synthesis[10] (Prins reaction) is the reaction of choice for the annulation of secolactaranes to lactaranes. The intramolecular version of the ene reaction was used several times in the past for the construction of a seven membered ring, starting from the appropriate unsaturated aldehyde.[11] To the best of our knowledge, however, the reaction with substrates where the formyl group is directly linked to a furan or a butenolide ring has no precedent. In the event, when lactaral (8) was treated with $SnCl_4$ as catalyst in various solvents (C_6H_6, CH_2Cl_2, CH_3NO_2) no cyclization took place and the furan compound was extensively decomposed. However, when lactaral was exposed to Me_2AlCl in a hexane-CH_2Cl_2 solution at r.t., in spite of the great instability of the furan system in acidic conditions, it was smoothly converted to a very non polar furan derivative (M^+ 214) to which the structure 10 has been assigned. The ^{1}H-NMR spectrum of the reaction product showed in fact two olefinic protons at 6.02 and 5.53 ppm and two signals at 6.93 and 7.12 ppm attributable to two furan protons. We never observed the appearance of an intermediate like 7, which was the expected first formed product of the ene reaction, but, evidently, could not survive under these conditions.

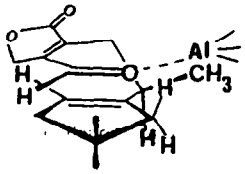
(*) For the sake of clarity the formulas already represent the absolute configuration which was finally assigned to the chiral centers.

The same diene 10, of identical rotatory power, was also obtained from furosardonin A (7), by stirring a benzene solution containing a catalytic amount of p-TsOH. These results were gratifying as they proved that both furosardonin A (7) and lactaral (8) have the same configuration at C-3, as required by the proposed mechanism of velutinals transformation.[7]



An analogous Me_2AlCl catalyzed ene cyclization was also successfully performed on the formyl secolactarane lactone 11 obtained by PCC oxidation of blennin C (9). The product of the reaction (35% yield) is the new lactone 12 having an "unnatural" stereochemical relationship between H-8 and H-9 and the C-3 methyl cis to H-9. In fact in the ^{1}H-NMR spectrum of compound 12 the small coupling constant (2.0 Hz) between H-8 and H-9 indicates a cis relationship between the latter protons, a value significantly greater ($\geqslant$ 8.0 Hz) being always found when H-8 and H-9 are trans diaxially oriented (see 17), as in natural lactarane lactones.[2] Moreover the methyl at C-3 must be pseudoequatorially oriented on the seven membered ring as its geminal proton shows an axial-axial coupling constant (J=11.2 Hz) with one of the protons at C-4. Finally $H\text{-}4_{ax}$ must be placed on the same side of the ring as H-9 (and H-8), on the basis of NOE experiments: the selective irradiation of H-9 produces in fact a 2.4% enhancement of the $H\text{-}4_{ax}$ signal, while the irradiation of $H\text{-}4_{ax}$ affects (2.6% NOE) the H-9 signal.

The diastereoselectivity thus exhibited by this intramolecular ene reaction is quite remarkable: an examination of the Dreiding models of the two possible transition states, 13 or 14, shows that the double bond π-face discrimination likely depends on a very unfavorable steric interaction between the C-3 methyl and the bulky $>C{=}O\cdots Al<$ complex, which is maximized in the transition state (13) where the two groups are closer.



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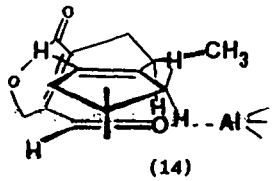
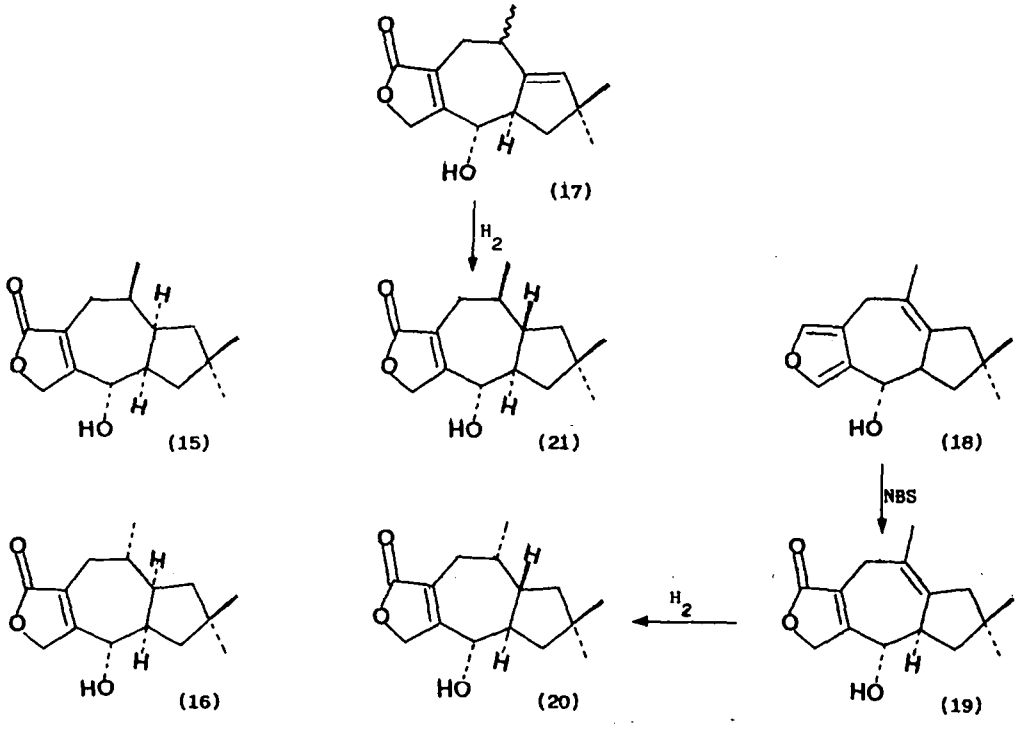


(14)

Correlation of furosardonin A (7) with lactarane lactones of established C-3 stereochemistry. Initially we planned to hydrogenate the cyclopentene double bond of furosardonin A in order to compare the 1,2-dihydroderivative with the furans obtained by the DIBAL-H reduction[12] of the two known lactones 15 and 16 having the two alternative C-3 configurations.[13,14] The double bond, however, could not be saturated without the simultaneous destruction of the furan ring, though various conditions and different catalysts were tested[25]. Then we resolved to oxidize the furan ring of furosardonin A to a less fragile α,β-unsaturated-γ-lactone. While sensitized photooxygenation of 7 (sunlight, aq. MeOH, Bengal rose as sensitizer), followed by $NaBH_4$ reduction of the formed γ-hydroxybutenolide gave the desidered product 17 in very low yield, on treatment with NBS in aq. dioxane[17] furosardonin A yielded the new sesquiterpene 17 in ca. 50% yield, no other isomer being formed in an appreciable amount. The structure 17 was indicated by the IR and NMR spectra, in particular the position of the carbonyl at C-5 and not at C-13 is supported by the following data: a long range homoallylic like coupling is observed between the $C(13)H_2$ and the $C(4)H_2$ protons, which is peculiar for 17 like structure[18], whereas it is impossible to attain for the isomeric C-13 lactones; furthermore by irradiation of the $C(4)H_2$ signals, no NOE enhancement is observed for the signals of the butenolide protons, as it is expected to occur for two groups too far away from each other, as in compound 17; finally an analogous oxidation of the known furanol 18, using the Wiesner procedure[17], yielded the known lactone 19[8c] as the only product. The remarkable siteselectivity of this furan ring oxidation is probably due to a coordination of the allylic C(8)-OH with an electrophilic Br^+ species which is supposed to promote the attack on the aromatic ring.[17b]



The catalytic hydrogenation of lactone 17 now proceeded without touching the heterocyclic ring, providing a new lactarane α,β-unsaturated lactone different (m.p., spectral data) from both the sesquiterpenes 15 and 16. Also the hydrogenation of compound 19 yielded a new stereoisomer of lactones 15 and 16. Since the four lactones 15, 16, 20 and 21 must have the same absolute

configuration at C-8 and C-9, for their common derivation from velutinals Ib-c, the structures of the hydrogenation products can differ from both reference lactones 15 and 16 only if the ring junction between the seven and five membered rings is trans, as in formulas 20 and 21. The former is thus assigned to the compound obtained by the syn hydrogen addition to the double bound of lactone 19, therefore the structure 21 must be attributed to the compound synthesized from furosardonin A. The C-3 methyl is then trans with respect to H-9 in all the compounds 17, 21 and 7, thus confirming the mechanism proposed for velutinals (1a-c) transformations.[7]

EXPERIMENTAL

All m.ps are uncorrected and were determined with a Fisher-Johns hot plate. Ir spectra were measured as films for oils or in KBr pellets for solids on a Perkin Elmer 197 spectrophotometer. PMR spectra were recorded with TMS as an internal standard at 80 MHz on a Bruker instrument or at 300.13 MHz on a Bruker CXP-300 spectrometer. The chemical shifts (δ,ppm) are reported for $CDCl_3$ (filtered through Na_2CO_3 to remove any acidic impurities) solutions unless otherwise stated. J are reported in Hz. NOE difference spectra were obtained by alternatively subracting right off resonance free induction decays (FIDS) from right on-resonance induced FIDS. NOE values reported in the text are only indicative. Electron impact (e.i.) mass spectra were determined on a Du Pont 21-492 B instrument at 70 eV. Specific optical rotations were measured on an automatic Perkin-Elmer polarimeter. Thin layer chromatographies were run on pre-coated silica gel (Merck 60 F_{254}) plates. The spots were detected under a 254 nm UV light source or by spaying with a vanillin-sulphuric acid solution and then heating the plates at 120°C for few min. Column chromatography (CC) was performed on Kieselgel 60 Merck (0.040-0.063 mm) silica gel. All reactions were run with magnetic stirring under an inert atmosphere of N_2 and those requiring anhydrous conditions were performed in oven-dried apparatus. Solvents and reagents were dried according to established procedures by distillation under N_2 from an appropriate drying agent: THF and dioxane ($LiAlH_4$); CH_2Cl_2 (CaH_2); C_6H_6 (Na). Dry solvents were stored over molecular sieves under N_2. DIBAL-H (1.0 M solution in toluene) and Me_2AlCl (1.0 M solution in hexanes) were purchased from Aldrich.

4-(2-(4,4-Dimethyl-1-cyclopentenyl)-propyl)-3-furanmethanol(lactarol, 5) by DIBAL-H reduction of 2-(2-(4,4-dimethyl-1-cyclopentenyl)-propyl)-3-hydroxymethyl-2-buten-4-olide (blennin C, 9). 101 µl of DIBAL-H solution were added by syringe to 16 mg (0.064 mmol) of blennin C (9) in THF (2 ml) at -15°C (Me_2CO-ice bath). After 1 hour the reaction was quenched with 10% H_2SO_4, diluted with Et_2O, washed with saturated aq. $NaHCO_3$ solution, then with brine, and finally dried over $MgSO_4$. After evaporation of the solvent, the residue was purified by silica gel CC. Elution with hexane-Me_2CO (4:1) gave 6 mg_9 (40% yield) of lactarol 5, $[\alpha]_D^{20}$ -4.0°($CHCl_3$, c=0.3), identical in all respects with reference data and an authentic sample.

2-(2-(4,4-Dimethyl-1-cyclopentenyl)-propyl)-3-formyl-2-buten-4-olide (11) by PCC[19] oxidation of blennin C (9). 117 mg (0.543 mmol) of freshly prepared PCC were added to 91 mg (0.364 mmol) of blennin C in CH_2Cl_2 (2 ml) containing anhydrous NaOAc. After stirring for 2h at r.t., the reaction mixture was diluted with anhydrous Et_2O, filtered through a $MgSO_4$- silica gel pad to remove the Cr salts and taken to dryness. The residue was purified by silica gel CC. Elution with hexane-AcOEt (9:1) gave 87 mg (64% yield) of compound 11, oil, $[\alpha]_D^{20}$ -8.97° ($CHCl_3$, c=1).
IR (cm^{-1}):3040, 2950, 2920, 2860, 2840, 1760 (lactone CO), 1685 (aldehyde CO), 1450, 1375, 1360, 1340, 1170, 1075, 1035, 985, 815, 760, 710.
PMR (80 MHz):1.02 and 1.05 (s and s, 3H and 3H, $(CH_3)_2$-C_{11}), 1.06 (d, 3H, J=7.0, CH_3-C_3), 2.09 (s, 4H, H-1, H-1', H-10, H-10'), 2.5-3.0 (m, 3H, H-3, H-4, H-4'), 4.92 (2H, br s, H-13, H-13'), 5.25 (1H, br s, H-9), 10.12 (1H, s, CHO).
MS, m/z(%):248 (M^+, 53), 233(85), 230(42), 220(18), 219(100), 215(45), 203(9), 201(13), 187(14), 174(10), 173(10), 160(12), 123(79), 122(60), 109(6), 107(28), 105(6), 95(28), 93(10), 91(12), 81(52), 79(12), 77(11), 69(11), 67(21), 57(10), 55(26), 53(16), 43(36), 41(59).

Dehydration of 4,4a,5,6,8,9-hexahydro-4-hydroxy-6,6,8-trimethylazuleno[5,6-c]furan (furosardonin A, 7) to 5,6,8,9-tetrahydro-6,6,8-trimethylazuleno[5,6-c]furan (10). A solution of furosardonin A (21 mg) in benzene, containing a catalytic amount of p-TsOH, was stirred at r.t. for 2 hours. The mixture was diluted with hexane, washed with 10% aq. Na_2CO_3 solution, brine and dried over $MgSO_4$. After evaporation of the solvents, the residue was purified by silica gel CC. Elution with hexane-Et_2O (15:1) gave 5.4 mg of furan 10, $[\alpha]_D^{20}$ -4.2°(Et_2O, c=0.4).[20] IR and UV data have already been reported.

PMR (80 MHz, C_6D_6): 1.04 and 1.06 (s and s, 3H and 3H, $(CH_3)_2$-C_{11}), 1.03 (d, 3H, J_{3-12}=7.2), 2.60 (m, 1H, H-3), centered at 2.5 (overlapped signals, 4H, H-4, H-4', H-10, H-10'), 5.53 (s, 1H, H-1), 6.02 (br s, 1H, H-8), 6.93 (br s, 1H, H-5), 7.12 (hidden by the solvent signal, 1H, H-13).
MS, m/z(%): 214(M^+, 65), 199(100), 156(14), 155(10), 143(14), 141(9), 129(9), 128(10), 115(8), 91(7), 84(8), 77(6), 41(12).

Ene cyclization of 4-(2-(4,4-dimethyl-1-cyclopentenyl)-propyl)-3-furancarbaldehyde (lactaral, 8) to furan 10. 153 µl of the Me_2AlCl solution were added to 35.6 mg of lactaral in 2 ml of CH_2Cl_2 chilled in an Me_2CO-ice bath. The mixture was then slowly taken to r.t. and stirred for 2 hours, finally quenched by few drops addition of 10% aq. Na_2CO_3 solution, diluted with hexane, washed with brine and dried over $MgSO_4$. Evaporation of the solvent and silica gel CC of the residue (eluant hexane-benzene, 15:0.5) gave 4.5 mg of furan 10, identical in all respects with the diene obtained by furosardonin A dehydration.

Ene ciclyzation of lactone 11 to 1,3,4,4a,5,6,8,9-octahydro-4-hydroxy-6,6,8-trimethylazuleno[5,6-c]furan-2-one (12). 101 µl of the Me_2AlCl solution were added to 25 mg of lactone 11 in 2 ml of CH_2Cl_2 at r.t. After 5 min the reaction was quenched with 10% aq. Na_2CO_3 solution and the mixture diluted with Et_2O, washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was chromatographed over silica gel (benzene-Me_2CO, 10:1 as eluant) to give 8.7 mg (35%) of lactone 12, m.p. 123°C, $[\alpha]_D^{20}$ -115° ($CHCl_3$, c=0.4).

IR (cm^{-1}):3440, 3020, 3945, 2915, 2850, 1740, 1675, 1625, 1125, 1100, 1080, 1040, 955, 840, 785, 755, 745.
PMR (300 MHz):1.06 and 1.14 (s and s, 3H and 3H, $(CH_3)_2$-C_{11}), 1.19 (d, 3H, J_{3-12}=6.8, CH_3-C_3), 1.77 (dd, 1H, $J_{10-10'}$=12.6, J_{10-9}=8.2, H-10), 1.93 (dd, 1H, $J_{10-10'}$=12.6, $J_{10'-9}$=8.5, H-10'), 2.19 (ddt, 1H, $J_{4-4'}$=16.5, J_{4-3}=11.2, $J_{4-13} \simeq J_{4-13'} \simeq$ 3, H-4), 2.6-2.43 (2H, overlapped multiplets, H-4', H-3), 3.33 (tq, 1H, $J_{9-10} \simeq J_{9-10'} \simeq$ 8.5, $J_{8-9}=J_{9-1} \simeq J_{9-3}$=2.0, H-9), 4.16 (br d, 1H, J_{8-9}=2.0, H-8), 4.65 (br dd, 1H, $J_{13-13'}$=17.2, J_{13-4} = 3.0, H-13), 4.94 (ddd, 1H, $J_{13-13'}$=17.2, $J_{13'-4}$=3.0, $J_{13'-4'}$=1.8, H-13'), 5.49 (t, $J_{1-9}=J_{1-3}$=2.0, H-1).
In C_6H_6 solution the signal of H-4'(2.43 ppm, dt, $J_{4-4'}$=16.2, $J_{4'-3}=J_{4'-13'}$=1.8) occurs well apart from that of H-3 (2.10 ppm, m).
MS, m/z(%):248(M^+, 15), 230(5), 215(11), 138(6), 123(30), 122(100), 121(7), 109(12), 108(8), 107(62), 105(8), 95(7), 93(11), 91(19), 79(11), 77(11), 55(11), 43(15), 41(22).

NBS oxidations: 1,3,4,4a,5,6,7,9-octahydro-4-hydroxy-6,6,8-trimethylazuleno[5,6-c]furan-2-one (anhydro deconjugated lactarorufin A, 19) and 1,3,4,4a,5,6,8,9-octahydro-4-hydroxy-6,6,8-trimethylazuleno[5,6-c]furan-2-one (17). N-Bromosuccinimide (NBS) (28 mg), freshly crystallized from H_2O, was added portionwise to a solution of furan 18 (33 mg) in dioxane (5 ml) and H_2O (100 µl). The reaction mixture was stirred at r.t. for 1h, diluted with H_2O and extracted with Et_2O. The solution was washed with aq. $NaHCO_3$, brine, dried ($MgSO_4$) and taken to dryness. The residue was chromatographed on silica gel (eluant: benzene-Me_2CO, 9:1) to give 19 (15 mg, 42%), identical to an authentic sample of the natural compound.
With the same procedure furosardonin A (7, 26.3 mg) was oxidized to the α,β-unsaturated-γ-lactone 17 (13 mg, 50%) sticky oil, $[\alpha]_D^{20}$ + 14.50°($CHCl_3$, c=0.3).

IR(cm^{-1}):3400, 1730, 1665, 1440, 1375, 1340, 1160, 1055, 845, 755.
PMR (300 MHz):1.09 and 1.14 (s and s, 3H and 3H, $(CH_3)_2$-C_{11}), 1.18 (d, 3H, J_{3-12}=6.8, CH_3-C_3), 1.74 (dd, 1H, $J_{10-10'}$=13.3, J_{10-9}=3.7, H-10), 1.92 (m, 1H, H-4, $J_{4-4'}$=15.4, J_{4-3}=11.0, $J_{4-13}=J_{4-13'}$=2.9, J_{4-8}=2.0, H-4), 2.04 (dd, 1H, $J_{10-10'}$=13.3, $J_{10'-9}$=8.5, H-10'), 2.19 (m, 1H, H-3), 2.68 (br dd, 1H, $J_{4-4'}$=15.4, $J_{4'-3}$=3.2, H-4'), 2.77 (dddt, 1H, J_{8-9}=10.5, J_{9-10}=3.7, $J_{9-10'}$=8.5, $J_{9-1} \simeq J_{9-3} \simeq$ 1.3, H-9), 4.43 (br d, 1H, J_{8-9}=10.5, H-8), 4.80 (dddd, 1H, $J_{13-13'}$= 18.2, J_{13-4}=2.9, $J_{13-4'}$=0.7, J_{13-8}=1.4, H-13), 4.90 (dddd, 1H, $J_{13-13'}$=18.2, $J_{13'-4}$=2.9, $J_{13'-4'}$=1.0, $J_{13'-8}$=1.6, H-13'), 5.47 (t, 1H, $J_{1-9} \simeq J_{1-3} \simeq$ 1.4, H-1).
MS, m/z(%):248 (M^+, 13), 230(8), 215(5), 123(23), 122(100), 109(12), 108(9), 107(44), 105(8), 94(7), 93(11), 91(19), 79(11), 77(10), 69(7), 55(9), 43(14), 41(18).

Catalytic hydrogenations: (4S,4aR,7aS,8S)-1,3,4,4a,5,6,7,7a,8,9-decahydro-4-hydroxy-6,6,8-trimethylazuleno[5,6-c]furan-2-one (20) and (4S,4aR,7aS,8R)-1,3,4,4a,5,6,7,7a,8,9-decahydro-4-hydroxy-6,6,8-trimethylazuleno[5,6-c]furan-2-one (21). A solution of anhydro deconjugated lactarorufin A(19, 35mg) in MeOH containing a catalytic amount of $HClO_4$ was hydrogenated over 10% Pd-C at r.t. and atmospheric pressure. After the theoretical amount of H_2 had been absorbed, solid Na_2CO_3 was added, then the solution was diluted with CH_2Cl_2, filtered to remove the catalyst and taken to dryness. The residue was crystallized from Me_2CO-hexane to give 20 mg of lactone 20, m.p. 166-168°C, $[\alpha]_{579}^{20}$+ 10.8° ($CHCl_3$, c=0.2).

IR (cm^{-1}):3555, 3430, 2945, 2865, 2840, 1720, 1665, 1440, 1365, 1345, 1295, 1265, 1220, 1200, 1170, 1145, 1115, 1090, 1045, 1020, 940, 880, 790, 770, 755, 685.
PMR (80 MHz):0.80 (d, 3H, J_{3-12}=7.0, CH_3-C_3), 1.05 and 1.15 (s and s, 3H and 3H, $(CH_3)_2$ C_{11}), 2.18-1.12 (overlapped signals of H-4, H-2, H-9, H-1, H-1', H-10, H-10'), 2.48-2.12 (m, 1H, H-3), 2.70 (dd, 1H, $J_{4-4'}$=15.8, $J_{4'-3}$=3.8, H-4'), 4.42 (br d, 1H, J_{8-9}=8.0, H-8), centered at 4.95 (br s, 2H, AB system, H-13 and H-13').

MS, m/z(%):250(M^+, 20), 235(9), 232(17), 223(14), 222(93), 221(14), 217(15), 207(15), 204(13), 191(8), 189(8), 175(8), 173(9), 137(12), 136(13), 135(12), 127(10), 125(11), 124(62), 123(29), 122(22), 121(11), 109(100), 107(16), 97(9), 95(53), 91(11), 83(11), 82(27), 81(26), 79(14), 77(10), 69(35), 68(20), 67(17), 65(8), 57(15), 55(50), 53(23), 43(43), 41(78).

With the same procedure the lactone **17** was hydrogenated to give the dihydroderivative **21**, oil, $[\alpha]_{579}^{20}$ -12° ($CHCl_3$, c=0.2).

IR (cm^{-1}):3400, 2940, 2920, 2860, 1730, 1670, 1445, 1380, 1365, 1345, 1080, 1045, 1025, 755.

PMR (80 MHz):0.97 (d, 3H, J_{3-12}=6.8, CH_3-C_3), 1.06 and 1.07 (s and s, 3H and 3H, $(CH_3)_2$-C_{11}), 2.0-1.12 (overlapped signals of H-1, H-1', H-10, H-10', H-4, H-2, H-9), 2.05 (m, 1H, H-3), 2.64 (dd, $H_{4-4'}$=16.0, $J_{4'-3}$=3.2, H-4'), 4.42 (br d, J_{8-9}=8.0, H-8), centered at 4.84 (br s, 2H, AB system, H-13, H-13').

MS, m/z(%):250(M^+,16), 235(6), 232(4), 223(7), 222(42), 221(11), 217(7), 207(9), 206(9), 205(8), 204(12), 191(6), 189(7), 177(7), 175(6), 173(7), 161(6), 153(6), 152(8), 149(7), 137(18), 136(15), 135(14), 127(10), 125(20), 124(55), 123(35), 121(15), 119(7), 110(11), 109(100), 107(15), 99(7), 97(10), 95(51), 93(12), 91(14), 85(13), 83(14), 82(21), 81(32), 79(18), 77(12), 69(31), 68(16), 67(19), 65(8), 57(7), 55(32), 53(19), 41(43).

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