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NEW CONGENERS OF CYTOTOXIC NOR-DITERPENOID DILACTONES IN PODOCARPUS NAGI: TWO C_{19} LACTONES FROM SEED EXTRACT

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In the preceding paper[1], we have presented the isolation of three highly oxygenated new members of nor- and bisnor-diterpenoid dilactones[2] in Podocarpus nagi Zoll. et Moritzi. Further investigation of the cytotoxic minor components[3] in seed endosperms permitted the isolation of additional two C_{19} dilactones, 1 and 2, which show Rf values (SiO_2 plate) comparable to those of nagilactone A (3) and C (5), respectively[4a~c]. The ir and uv spectra indicated the presence of two lactone groups, an α-pyrone group (λ_{max} 300 nm, ν_{max} 1700, 1620, 1540 cm^{-1}) and a γ-lactone group (ν_{max} 1760~1780 cm^{-1}), in both of the components, as reported for the related dilactones[1,4].

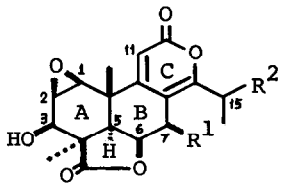
The compound (1), mp 238~9°, $C_{20}H_{22}O_8$, m/e(20 eV) 390(M^+,64), 359(22), 331 (57), 303(100), 289(49), 288(47), 260(31), 247(19), 229(23), 201(34); $[\theta]^{MeOH}_{295nm}$ +11100, has a methoxycarbonyl group, which is proved by pmr (OCH_3: 3.58 ppm), cmr (CO: 170.4 ppm; two lactone carbonyl groups: 162.5, 177.7 ppm) and ir (1730 cm^{-1}) spectra. Mass fragment peaks, m/e 359(M^+-OCH_3) and 331(M^+-CO_2CH_3), also supported this fact. The pmr spectrum of 1 closely resembles ($\Delta\delta < 0.1$ ppm) that of nagilactone D (6)[4a] in whole region, except for the signals due to near-by protons to the methoxycarbonyl group. Thus, a two-proton quartet (2.47 ppm) and a three-proton triplet (1.10 ppm) in 6 are replaced by a one-proton quartet (4.26 ppm) and a three-proton doublet (1.60 ppm), respectively.

The signals of H-7α and H-7β also displace (0.2∼0.3 ppm) to lower field in the compound (1). Therefore, 15-methoxycarbonyl-nagilactone D is proposed for the structure of 1. The stereochemistry at C-15 remains undetermined.

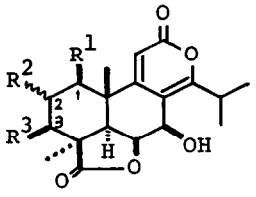
The compound (2), mp 243∼5°(dec), $C_{19}H_{24}O_6$, m/e(20 eV) 348(M^+, 100), 320 (96), 305(79), 287(29), 277(32), 259(25), 245(20), 231(10), 215(15), 213(16), 205(24), 203(17), 189(25); $[\theta]^{MeOH}_{293nm}$ +3980, gave a diacetate, $C_{23}H_{28}O_8$, m/e(20eV) 432(M^+). The fragmentation of 2 by electron impact is closely similar to that of nagilactone A (3)[8]. Three methine hydrogens, H-5α, H-6α and H-7α, are correlated to each other by pmdr. The chemical shift of H-7α (the carbinyl proton of one hydroxyl group) at unusually low field (5.54 ppm in 2; 6.73 ppm in diacetate) shows that the proton should be at an adjacent position to the pyrone ring. The second hydroxyl group is placed at 2α-position from the following reasons: (i) The compound (2) is different from nagilactone A (3) or sellowin C (7)[6] by pmr and mp comparisons; this fact eliminates a possibility of 1β or 3β position. (ii) The carbinyl proton of this hydroxyl group couples with four adjacent methylene protons at C-1 and C-3 (parameters are shown in Table 1), and appears in a very broad multiplet signal ($W_{1/2} \simeq 40$ Hz). Since the ring A of 2 should take a chair form[4c,5], the carbinyl hydrogen must be at 2β (axial). (iii) Practically no acetylation-shift of the H-11 signal is observed in a conversion of 2 (6.20 ppm) to the diacetate (6.15 ppm), while the corresponding signal of the related lactones with 1β-hydroxyl group shows a large high-field shift (0.9∼1.3 ppm, in pyridine) on acetylation[1,4a]. Thus, 1-deoxy-2α-hydroxy-nagilactone A is proposed for the structure of 2.

The absolute configuration of the two components should be the same as those of nagilactone A (3) and B (4)[4c], as shown in the formula, since the same sign of Cotton effect was obtained by cd measurements.

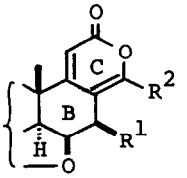
There have been known three major types, I, II and III, of B/C ring system in naturally occurring Podocarpus dilactones, although the biogenetic preference of each type in intact plant tissues is still unknown. It should be interesting that only the type I dilactones (nine lactones[1,4a] including two, reported here) have been found from seed endosperms of Podocarpus nagi, while the root bark mainly contains other two types[4d,7], II and III.



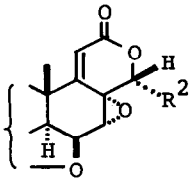
(1) R^1=H, R^2=CO_2CH_3
(5) R^1=OH, R^2=CH_3
(6) R^1=R^2=H



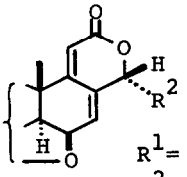
(2) R^1=R^3=H, R^2=α-OH
(3) R^1=OH, R^2=R^3=H
(4) R^1=OH, R^2=β-OH, R^3=H
(7) R^1=R^2=H, R^3=OH



(I)



(II)



(III)

R^1= H or OH
R^2= Alkyl

Table 1. The pmr parameters of the lactones (pyridine-d_5).

Lactones	CH_3^*	CH_3^{**}	H^1	H^2	H^3	H^5	H^6	$H^{7\beta}$	$H^{7\alpha}$	H^{11}	H^{15}
(1)#	1.44 1.52	1.60 (7.5)	3.71 d (4.0)	3.60 dd (4.0, 6.0)	4.64 d (6.0)	1.96 d (6.5)	4.98 dt (6.5, 6.5, 9.5)	2.96 dd (6.5, 17.0)	3.65 dd (9.5, 17.0)	6.72 s	4.26 qua (7.5)
(6)	1.44 1.51	1.10 t (7.5)	3.68 d (4.0)	3.52 dd (4.0, 6.0)	4.61 d (6.0)	1.88 d (6.5)	4.89 dt (6.5, 6.5, 10.0)	2.71 dd (6.5, 17.0)	3.34 dd (10.0, 17.0)	6.56 s	2.47 qua (7.5)
(2)	1.40 1.76	1.23 (7.0) 1.30 (7.0)	***	4.25 br m	***	1.78 d (6.5)	5.03 dd (6.5, 8.5)	--	5.54 d (8.5)	6.20 s	3.41 m (7.0)
(2)-Ac_2	1.36 1.47	1.10 (7.0) 1.14 (7.0)	5.2 -----	5.2 br s	5.2 ----	1.90 d (6.5)	5.28 dd (6.5, 9.0)	--	6.73 d (9.0)	6.15 s	3.06 m (7.0)
(3)	1.33 2.01	1.26† (6.6)	4.1 br	--	--	1.83 d (5.7)	5.17 dd (5.7, 8.6)	--	5.67 d (8.6)	7.38 s	3.51 m (6.6)
(3)-Ac_2	1.24 1.55	1.13 t† (7.0)	5.18 br t	--	--	1.94 d (5.5)	5.30 dd (5.5, 8.5)	--	6.62 d (8.5)	6.03 s	3.09 m (7.0)
(7)[6b]	1.32 1.98	1.28 t† (6.0)	2.52 m 1.60 m	2.08 m 1.94 m	4.16 br t	1.84 d (6.0)	5.14 dd (6.0, 8.0)	--	5.64 d (8.0)	7.32 s	3.48 m

* singlet methyl signals. ** doublet methyl signals unless otherwise specified. *** H-1β: 2.14 ppm, H-1α: 2.58 ppm, H-3β: 1.95 ppm, H-3α: 2.45 ppm. $J_{2\beta,1\beta}$=5.5, $J_{2\beta,1\alpha}$= 13.5, $J_{1\beta,1\alpha}$= 13.5, $J_{2\beta,3\beta}$= 6.5, $J_{2\beta,3\alpha}$= 9.5, $J_{3\beta,3\alpha}$=13.5 Hz.
# methoxyl signal: 3.58 ppm (3H, s). † overlapped signals.

s: singlet, d: doublet, t: triplet, dd: double doublet, dt: double triplet, qua: quartet, m: multiplet, br: broad.

Footnotes and References

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