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LINARIDIAL, A NEW CIS-CLERODANE-TYPE DITERPENE DIALDEHYDE, FROM LINARIA JAPONICA MIQ.

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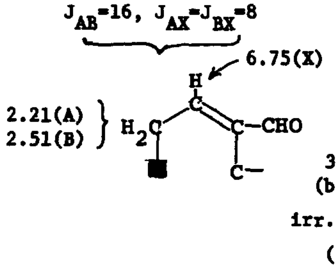
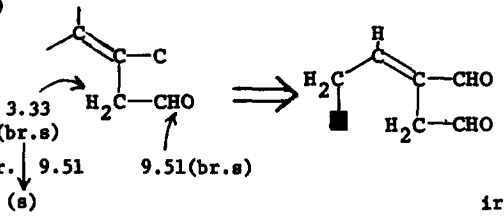
Recently we reported the structure elucidation of a new chlorinated iridoid glucoside named linarioside which was isolated from *Linaria japonica* Miq.(*Scrophulariaceae*)1). In a continuative study on the constituents of the same plant, we have isolated a new diterpene dialdehyde named linaridial, to which the structure **1** is now assigned on the basis of the following evidence. Linaridial(**1**) seems to be the first diterpene possessing a *cis*-clerodane skeleton elucidated from the scrophulariaceous plants.

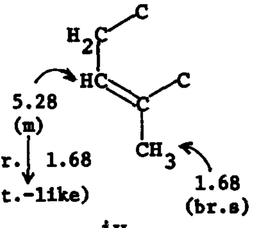
Dry column chromatography(silica gel) of the ether extractive of fresh subterranean part gave linaridial as an unstable oily substance in a 9 % yield(from the extractive). Linaridial (**1**), $C_{20}H_{30}O_2$(M^+)2), $[\alpha]_D$ +13°($CHCl_3$), reduces the red tetrazolium and $AgNO_3/NH_4OH$ reagents. It possesses an aldehyde(IR(CCl_4): 2750, 1728 cm^{-1}; PMR3): 9.51(1H, br.s)) and a conjugated aldehyde function(UV: λ_{max}^{ether} 235 nm(ε, 11,300); IR(CCl_4): 1683, 1638 cm^{-1}; PMR: 9.40(1H, s)). The PMR examination of **1** including the spin decoupling experiments has led to the partial structures **i** and **ii** which are further combined as **iii**. The 1,4-dial structure(**iii**) has also been supported by preparing a bis-2,4-dinitrophenylhydrazone(**2**), $C_{32}H_{38}O_8N_8$4); mp 207-209°; IR(Nujol): 3430, 3310, 1620, 1595, 1329 cm^{-1}, which is a sole crystalline derivative of linaridial. Linaridial(**1**) shows four methyl signals in its PMR spectrum: one secondary(0.82, d, J=6), two tertially(0.93, 1.02, each s), and one olefinic(1.68, br.s, $W_{h/2}$=5) methyls, of which the latter is coupled with an olefinic proton as depicted in the partial structure **iv**. Based on the above evidence, a clerodane-type(A)(eg. kolavenic acid5)) or a perhydroazulene(B)



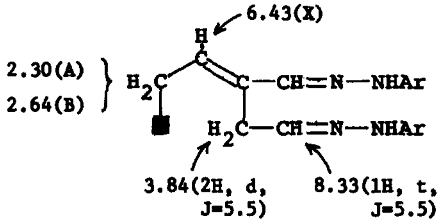
i



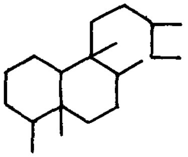
ii iii



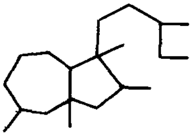
iv



2 PMR(d_5-py.)



A

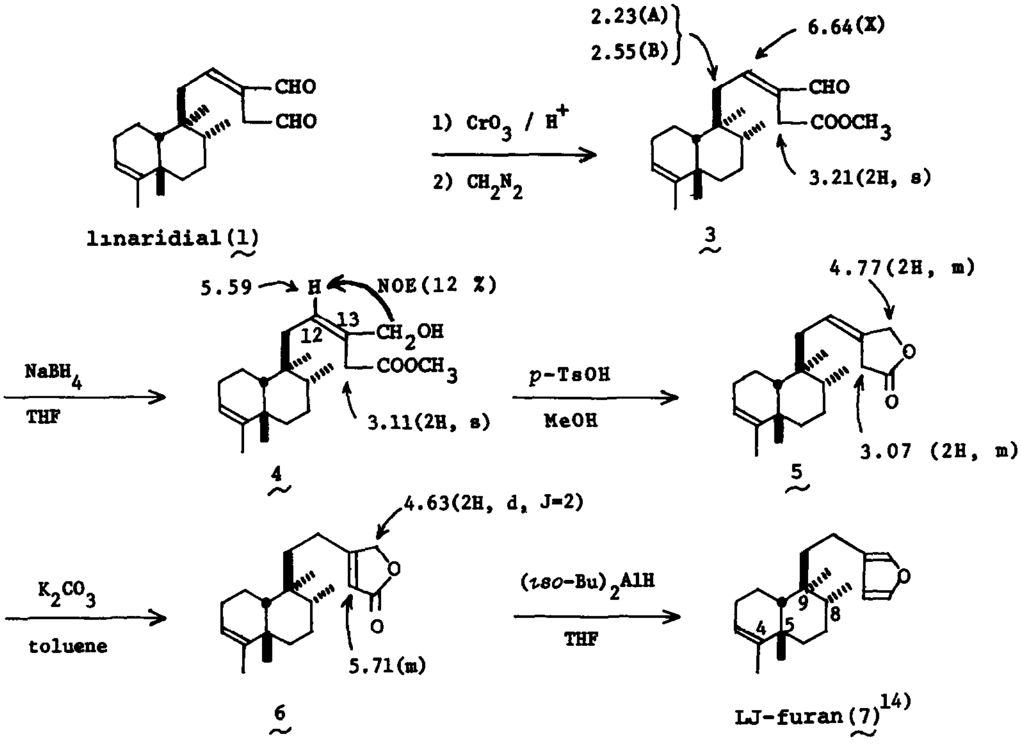


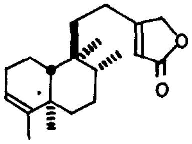
B

(eg. portulal[6]) skeleton has been advanced as the possible carbon framework of linaridial.

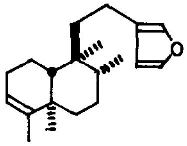
On $CrO_3/H_2SO_4/H_2O$ oxidation followed by CH_2N_2 methylation, 1 gave an ester-aldehyde(3), $C_{21}H_{32}O_3(M^+)$; UV: λ_{max}^{ether} 234.5 nm(ε, 13,900); IR(CCl_4): 2710, 1746, 1690, 1640 cm^{-1}; PMR: 3.63 (3H, s), 9.36(1H, s), which was converted with $NaBH_4$/THF to an ester-ol(4), IR(CCl_4): 3350, 1747 cm^{-1}. In the PMR spectrum of 4, an NOE(12 %) of the 12-H signal was observed on irradiation at δ 4.03(13-$C\underline{H}_2$OH), thus proving the geometry of Δ^{12}. Mild *p*-TsOH/MeOH treatment of 4 furnished a γ-lactone(5), $C_{20}H_{30}O_2(M^+)$; UV(ether): transparent above 210 nm; IR(CCl_4): 1788 cm^{-1}, which on heating with K_2CO_3/dry toluene[7] was isomerized to a butenolide(6), $C_{20}H_{30}O_2(M^+)$; $[\alpha]_D$ +23.5°(EtOH); UV: λ_{max}^{EtOH} 222 nm(ε, 8,600); IR(CCl_4): 1780, 1750, 1639 cm^{-1}. Furthermore, (*iso*-Bu)$_2$AlH/THF reduction[8] of 6 furnished LJ-furan(7), $C_{20}H_{30}O(M^+)$; $[\alpha]_D$ +32°(EtOH); IR(CCl_4): 872 cm^{-1}; PMR: 6.09, 7.04, 7.16(1H each, narrow m); m/e(%): 191(100)(v)[9], 95(82)(vi)[10], 81(77)(vii)[10]. All of these derivations are well explained on the basis of the side chain structure (iii). As for the ring system, the abundant ion peak at m/e 191(v), observed in the mass spectra of linaridial(1) and its derivatives, is suggestive for the clerodane skeleton[9].

Finally, the comparison of the PMR data(especially the chemical shift differences of the methyl signals) of 6 and LJ-furan with those of solidagolactone(8), $[\alpha]_D$ -78.4°[11], *trans*(9)[12]

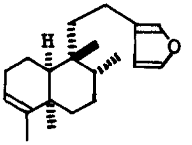




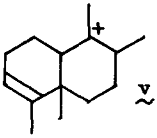
solidagolactone (8)[11]



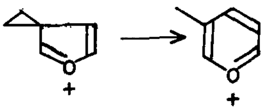
9[12]



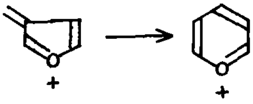
10[13]



v m/e 191 $C_{14}H_{23}$



m/e 95 vi



m/e 81 vii

Table I. PMR Data (δ values in CCl_4)

	$4-CH_3$	$5-CH_3$	$8-CH_3$	$9-CH_3$
6	1.68	1.03	0.78	0.84
8[11]	1.57	1.01	0.84	0.77
LJ-furan	1.65	1.02	0.78	0.80
9[12]	1.57	1.00	0.86	0.74
10[13]	1.64	1.17	0.92	1.08

and *cis*(10)[13] furano-clerodanes has led us to assume that LJ-furan may be identical with another *cis*-furano-clerodane(7), $[\alpha]_D$ +33°, which has recently been reported by McCrindle, *et al.*[14] The direct comparison of both undertaken by Dr.R.McCrindle has verified the assumption, and the stereostructure 1 has now been established for linaridial.

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FOOTNOTES AND REFERENCES:

1) I.Kitagawa, T.Tani, K.Akita and I.Yosioka, *Chem.Pharm.Bull.*(Tokyo), 21, 1978 (1973); *Tetrahedron Letters*, 1972, 419. 2) The compositions of the compounds given with M^+ were confirmed by high resolution mass spectrometry. 3) Taken in CCl_4 at 90 MHz, the chemical shifts in ppm, and J and $W_{h/2}$ values in Hz. 4) Satisfactory analytical value was obtained. 5) R.Misra, R.C.Pandey and S.Dev, *Tetrahedron Letters*, 1964, 3751. 6) S.Yamazaki, S.Tamura, F.Marumo and Y.Saito, *Tetrahedron Letters*, 1969, 359. 7) I.Kitagawa, H.Shibuya, Y.Yamazoe, H.Takeno and I.Yosioka, *Tetrahedron Letters*, 1974, 111. 8) H.Minato and T.Nagasaki, *J.Chem. Soc.*(C), 1966, 377. 9) a)M.Ferrari, F.Pelizzoni and G.Ferrari, *Phytochemistry*, 10, 3267 (1971); b) P.R.Jefferies, J.R.Knox and B.Scaf, *Aust.J.Chem.*, 26, 2199 (1973). 10) F. Bohlmann, M.Grenz and H.Schwarz, *Chem.Ber.*, 106, 2479 (1973). 11) T.Okazaki, A.Ohsuka and M.Kotake, *Nippon Kagaku Zasshi*, 1973, 584. 12) K.Kawazu, C.Nishino, R.McCrindle, and D.McMaster, *Agr.Biol.Chem.*, 36, 1245 (1972). 13) T.Anthonsen, M.S.Henderson, A.Martin, R.D.H.Murrary, R.McCrindle and D.McMaster, *Can.J.Chem.*, 51, 1332 (1973). 14) A.B.Anderson, R.McCrindle and E.Nakamura, *Chem.Commun.*, 1974, 453.