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LAPPAOL A AND B, NOVEL LIGNANS FROM ARCTIUM LAPPA L

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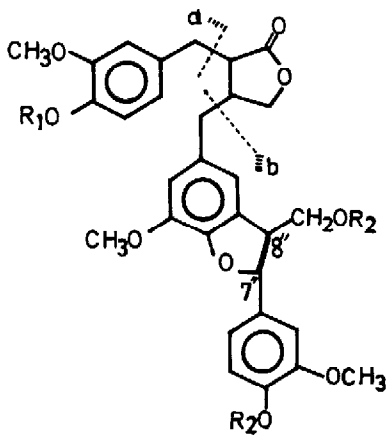
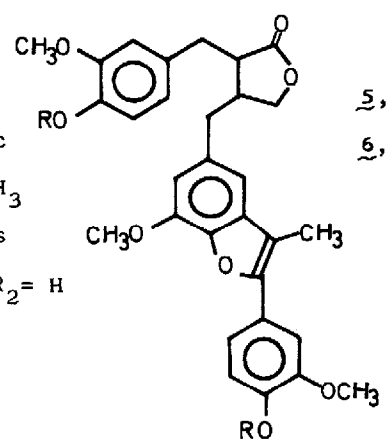
The roots of Arctium lappa L (gobo in Japanese) are widely used as a food in Japan and the seeds are known as one of folk medicines. From the seeds two new compounds, lappaol A (1) and B (7), were isolated. In this communication, we should like to describe the structural determination of these novel lignans.



1, R_1, R_2= H
2, R_1, R_2= Ac
3, R_1, R_2= CH_3
4, R_1, R_2= Ms
10, R_1= CH_3, R_2= H



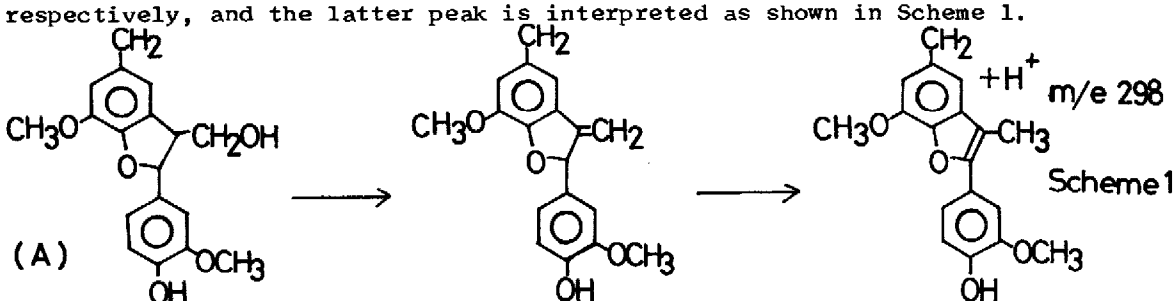
5, R= Ms
6, R= H

Lappaol A, $C_{30}H_{32}O_9$ (amorphous, m/e M^+ found 536.2024, calcd. 536.2043) showed following physical and spectral properties; $[\alpha]_D^{20}$ -17.4° (c 1.0, CH_3OH); UV $\lambda_{max}^{CH_3OH}$ 283nm (ε 7800); IR ν_{max}^{KBr} 3400, 1760, 1600, 850, 805 cm^{-1}; NMR (90MHz), $\nu_{TMS}^{CDCl_3}$ 2.56 (4H, m, $ArCH_2$-), 2.90 (2H, m, -CHCH-), 3.60 (3H, m, -CH_2OH), 3.83 (3H, s, OCH_3), 3.88 (6H, s, OCH_3), 4.16 (2H, m, $-CH_2OCO-$), 5.55 (1H, d, J=7Hz, CH-O), 5.70 (OH), 6.46~7.02 (8H, m, ArH). Since the absorption inten-

sity of 1 in the UV spectrum is one and a half stronger than that of arctigenin[1] (ε 5200), lappaol A would have three aromatic rings. A strong peak at 1760 cm^{-1} in the IR spectrum indicates the presence of a γ-lactone in 1. The NMR spectrum is very similar to that of arctigenin besides the signals at δ3.60, 5.55 and 6.46~7.02. The former two signals were assigned as 8"-H and 7"-H on dihydrofuran ring, based on the analogy with other similar compounds.[2]

Acetylation of 1 gave a triacetate 2, $C_{36}H_{38}O_{12}$ (m/e M^+ found 662.2324, calcd. 662.2360), which exibited signals at δ2.30, 2.28 (each 3H) ascribable to two phenolic acetates and at δ2.10 (3H) due to an alcoholic acetate. The fact that the signal at δ3.60 (2H) in the NMR spectrum of 1 shifts to lower field (δ4.36) in the acetate 2 suggests the presence of a hydroxymethyl group. Methylation of 1 with dimethyl sulfate gave a permethylated compound, 3, $IR\nu_{max}^{film}$ 1760, 1600, 850, 800 cm^{-1}; NMR (90MHz), $\delta_{TMS}^{CDCl_3}$ 2.56 (4H, m, $ArCH_2$-), 2.94 (2H, m, -CHCH-), 3.74 (1H, m, -OCH-CH-), 3.76 (3H, s, OCH_3), 3.85 (6H, s, OCH_3), 3.87 (9H, s, OCH_3), 4.12 (2H, m, $-CH_2$-OCO), 4.42 (2H, m, $C-CH_2O$), 5.52 (1H, d, J=7Hz, -OCH-CH-), 6.40~7.00 (8H, m, ArH).

The mass spectrum of 1 provided fruitful information on the structure. Significant peaks at m/e 137 and 298 corresponds to cleavages a and b-H_2O+H^+ respectively, and the latter peak is interpreted as shown in Scheme 1.

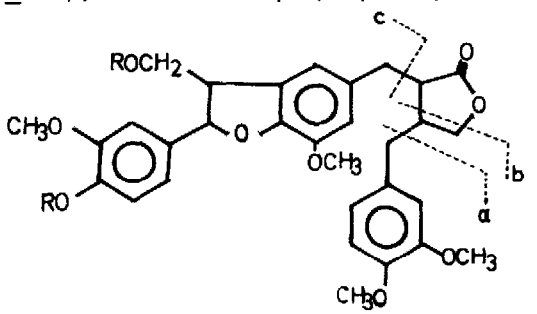


Scheme 1

Chemical conversion according to this fragmentation pattern was realized. Lappaol A was mesylated by mesyl chloride-pyridine to a trimesylate 4, NMR (90MHz), $\delta_{TMS}^{CDCl_3}$ 3.10, 3.15, 3.18 (each 3H, s, $SOCH_3$), which was treated with

diazabicycloundecane to yield a dimesylate 5; NMR (90MHz), $\delta_{TMS}^{CDCl_3}$ 2.40 (3H, s, $=C-CH_3$), 3.10, 3.21 (each 3H, s, $SOCH_3$). The dimesylate 5 was then hydrolized with potassium hydroxide to give a benzofuran 6 UV$\lambda_{max}^{CH_3OH}$ 309nm (ε 25000), IRν_{max}^{film} 3400, 1760, 1600, 850, 800 cm^{-1}; NMR (90MHz), $\delta_{TMS}^{CDCl_3}$ 2.36 (3H, s, $=C-CH_3$), 2.62 (4H, m, $ArCH_2-$), 2.90 (2H, m, -CHCH-), 3.70 (3H, s, OCH_3), 3.96 (6H, s, OCH_3), 4.12 (2H, m, $-CH_2O$), 5.49 (OH), 5.78 (OH), 6.34~7.24 (8H, m, ArH). The mass spectrum of 6 shows intense ions at m/e 137, 298, which are also observed in the spectrum of lappaol A. These observation clearly proves the presence of moiety (A) in 1. Other peaks at m/e 194, 220, 221 in 1 were particularly significant.[3] They could not have arisen from the alternative structure, in which the aryl groups were interchanged. The phenolic hydroxyl groups and methoxyl groups were placed as shown in 1 on the findings that lappaol A (1) gave a negative Gibbs test and has a strong absorption at 3550 cm^{-1} due to intramolecular hydrogen bond ($-OH\cdots O-^{CH_3}$)[4] and all the substituent patterns are in accord with biogenetic consideration.

Lappaol B (7) $C_{31}H_{34}O_9$ (m/e M^+ 550), $[\alpha]_D^{20}$ -19.4°(c 1.0, CH_3OH) is very similar to lappaol A (1) in spectral properties. UV$\lambda_{max}^{CH_3OH}$ 282 (ε 7460); IRν_{max}^{film} 3400, 1760, 1600, 850, 800 cm^{-1}; NMR (90MHz), $\delta_{TMS}^{CDCl_3}$ 2.53 (4H, m, $ArCH_2-$), 2.91 (2H, m, -CHCH-), 3.52 (3H, m, -CHCH$_2$OH), 3.78 (3H, s, OCH_3), 3.84 (6H, s, OCH_3), 3.86 (3H, s, OCH_3), 4.12 (2H, m, $-CH_2OCO-$), 5.50 (1H, d, J=7H, -O-CHCH-), 6.48~6.94 (8H, m, ArH). Acetylation of lappaol B (7) gave a diace-



7, R= H
8, R= Ac
9, R= CH_3

tate 8, IR ν_{max}^{film} 1760, 1740 cm^{-1}; NMR (90MHz), $\delta_{TMS}^{CDCl_3}$ 1.95 (3H, s, $COCH_3$), 2.21 (3H, s, $COCH_3$). Methylation of lappaol B (7) afforded a permethylated compound 9, IR ν_{max}^{film} 1760, 850, 800 cm^{-1}; NMR (90MHz), $\delta_{TMS}^{CDCl_3}$ 2.58 (4H, m, $ArCH_2$-), 2.94 (2H, m, -CHCH-), 3.73 (1H, m, -CH-CH_2OH), 3.74 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.90 (6H, s, OCH_3), 3.92 (6H, s, OCH_3), 4.12 (2H, m, $-CH_2OCO-$), 4.42 (2H, d d, J=6Hz, 3Hz, C-CH_2-OH), 5.50 (1H, d, J=7Hz, O-CH-CH), 6.47~7.00 (8H, m, ArH), which was almost identical with methylated lappaol A 3 in the IR spectrum and the behavior on TLC, but slightly different in the NMR spectrum, especially in aromatic region. A decision in favour of structure 7 for lappaol B was reached from a consideration of the mass spectrum which shows the peaks at m/e 151, 177, 298 derived from cleavage a, b and c-H_2O+H^+, in which fragment b could not arisen from alternative structure, i. e. methyllappaol A (10).

Biogenetically, lappaol A and B would be derived from matairesinol and arctigenin respectively and classified as lignan.[5] General term "sesquilignan" is proposed for them, since these may be formed by trimerisation of p-hydroxyphenylpropene units, compared with usual lignan derived from dimerisation.

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