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THE STRUCTURE OF POTAMOGETONIN

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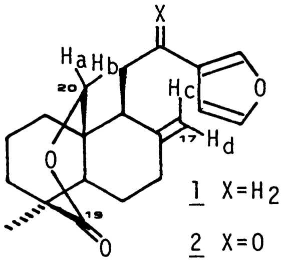
By conversion of methyl 15,16-epoxy-20-oxo-8(17),13(16),14 labdatrien-19-oate (3) into 15,16-epoxy-8(17),13(16),14-labdatrien-19,20-olide (1)and 15,16-epoxy-8(17),13(16),14-labdatrien-20,19-olide (8), the structure of potamogetonin was proved to be 15,16-epoxy-8(17),13(16),14-*ent*-labdatrien-20,19-olide (10), not 1 as proposed by Smith *et al.*

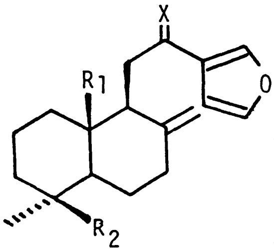
Potamogetonin has been isolated from seeds of *Potamogeton ferrugineus*, and the chemical structure 1 or its enantiomer has been proposed by Smith *et al.*[1)]

Recently we investigated the chemical constituents of seeds of *Sciadopitys verticillata* and isolated a new diterpenoid, methyl 15,16-epoxy-20-oxo-8(17),13(16), 14-labdatrien-19-oate (3) together with a number of closely related labdane-type diterpenoids including sciadin, sciadinone (2) and dimethyl sciadinonate which had been isolated from the heartwood of the same plant by Sumimoto [2)] and Kaneko *et al.*[3)] The physical constants of 3 are as follows : $[\alpha]_D^{20}$ +36.2° (c=0.58,$CHCl_3$); MS m/z (rel. int.): 344(M^+,98),316(30),313(23),255(22),175(60),161(66),81(100); IR ν_{max}^{neat} cm^{-1}: 2750,1705(aldehyde),1720,1160(methoxy carbonyl),3080,894(exomethylene),3135, 1503,874(furan); ^1H NMR δ(100MHz,$CDCl_3$,J:Hz): 9.65(1H,d,J=1.7),7.29(1H,dd,J=1.8,1.7), 7.12(1H,m),6.19(1H,dd,J=0.9,1.8),4.96,4.65(each 1H,s),1.23,3.56(each 3H,s). The ^{13}C NMR spectrum of 3 revealed signals very similar to those of known methyl 12,20-dioxo -lambertianate (4) [4)] except for signals for C-9,11,12,13,14,15 and 16.(see the Table) Thus, an aldehydic and a methoxycarbonyl groups in 3 were deduced to be located at C-10β and C-4β of a labdane skeleton, respectively. Furthermore, the fact that the signal for a methyl group at C-4α was observed at δ 1.23 in the ^1H NMR of 3 confirmed the above deduction, since the chemical shift due to C-4α methyl group was observed at δ 1.17-1.23, in 4, mehtyl lambertianate [5)] and methyl isocupressate [6)], all of



1 X=H_2

2 X=O



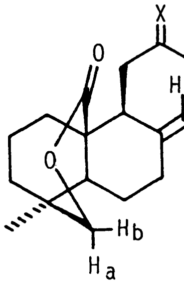
3 X=H_2 } R_1=CHO

4 X=O } R_2=$COOCH_3$

5 X=H_2 R_1=$COOCH_3$ R_2=CHO

6 X=H_2 } R_1=R_2=CH_2OH

7 X=O



8 X=H_2

9 X=O

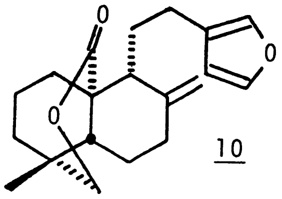
which had a methoxycarbonyl group at C-4β, on the other hand, isoagatholal 7), agathalic acid 8) and torulosal 9), possessing an aldehydic group at C-4β showed the signal for C-4α methyl group at δ1.02-1.00. Therefore, the structure of 3 was established as methyl 15,16-epoxy-20-oxo-8(17),13(16),14-labdatrien-19-oate, and the isomeric structure, 5, was denied. Reduction of 3 with $NaBH_4$ in methanol afforded a lactone(1) without formation of the corresponding 20-hydroxyl derivative, almost quantitatively. [1 ; colorless oil; $[\alpha]_D^{20}$ +8.7°,$[\alpha]_{400}$+20.5°,$[\alpha]_{300}$+47.6°, $[\alpha]_{260}$+59.3°(c=0.41,MeOH); MS m/z(rel. int.): 314.1879(M^+,100)(calcd for $C_{20}H_{26}O_3$: M,314.1882),233(24),94(94),82(72),81(49); IR $\nu_{max}^{CCl_4}$ cm^{-1}:1735,1140(δ-lactone),1025, 896,867; ^1H NMR δ(100MHz,$CDCl_3$,J:Hz):7.31(1H,dd,J=1.6,1.6,H-15),7.15(1H,m,H-16), 6.21(1H,dd,J=0.9,1.6,H-14),5.03(1H,d,J=1.2,H_d-17),4.68(1H,s,H_c-17),4.36(1H,dd,J= 2.2,12.0,H_b-20),4.00(1H,dd,J=1.0,12.0,H_a-20),1.17(3H,s,H-18); ^{13}C NMR: see the Table]. On the basis of these spectral data, the structure of the lactone was determined as 1 proposed for potamogetonin. However, the ^1H and ^{13}C NMR spectra of the synthetic 1 differed from those reported by Smith. The conclusive difference in ^1H NMR between chemical shifts of C-18 mehtyl groups in the synthetic 1 (δ 1.17) and potamogetonin (δ 0.87) was observed. Therefore it was considered that Smith's structural formula had to be reexamined, and an alternative structure 8 for potamogetonin was supposed. An attempt to synthesize 8 was made as follows. Reduction of 3 with $LiAlH_4$ afforded a diol 6, [6: colorless needles, mp 86.0-86.5°C, $[\alpha]_D^{20}$+19.1° (c=3.14,$CHCl_3$); MS m/z: 318(M^+); IR ν_{max}^{KBr} cm^{-1}: 3320,1024,1640,895,1505,875,757; ^1H NMR δ(60MHz,$CDCl_3$):7.27,7.13,6.23(furan),4.92,4.78(exomethylene),3.72,3.60(each 2H, s,-$C\underline{H}_2OH$),1.00(3H,s,H-18)], which was oxidized with Sarett's reagent to give a mixture of lactones, 1 and 8 (ca 1:19) in 85% yield. This result indicated that the hydroxymethyl group at C-10 was much more reactive with Sarett's reagent than the one at C-4, and, as a consequence, 8 was mainly formed. The similar result was recognized when 7 was oxidized to yield 2 and 9 (ca 1:7).$^{3)}$ [8: mp 99-100°C(recrystallized from pentane); $[\alpha]_D^{20}$ +37.5°,$[\alpha]_{400}$+85°,$[\alpha]_{300}$+197°,$[\alpha]_{250}$+412°,$[\alpha]_{230}$+485° (c=0.40,MeOH); MS m/z (rel. int.): 314(M^+,100),147(33),95(27),94(43),81(20); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1745,1133(δ-lactone),1051,1025,899,8070; ^1H NMR δ(100MHz,$CDCl_3$,J:Hz): 7.29(1H,dd,J=1.6,1.6,H-15),7.15(1H,m,H-16),6.23(1H,dd,J=0.9,1.6,H-14),4.93(1H,d,J=1.1,H_d-17),4.80(1H,s,H_c-17),4.13(1H,dd,J=1.5,12.0,H_b-19),3.99(1H,d,J=12.0,H_a-19), 0.89(3H,s,H-18)]. The IR, ^1H NMR spectral data for 8, obtained, was in good agreement with those reported by Smith. Furthermore, in the ^{13}C NMR spectrum of 8 the chemical shifts for the carbon atoms were in good agreement with the values published for potamogetonin, although there were some inconsistencies between our and Smith's assignments (Table). Our assignments have been based on the following consideration. The methylene signal at δ 25.8, ascribed to C-3 by Smith was assigned to C-12 by comparing the spectra of 8 and 9, where δ 25.7 was replaced by δ 194.6 due to the carbonyl carbon atom. The other two methylene signals at δ 36.0 and 36.9 were

Table ^{13}C chemical shifts of potamogetonin, 1, 3, 4, 8 and 9

	1	3	4	8	potamogetonin	9
C-1	37.8	31.8	31.6	41.0	41.1	41.1
2	21.1	20.5	20.4	20.9	20.9	20.9
3	39.9	38.8	38.9	36.0	25.8	36.3
4	43.6	45.6	45.6	33.4	33.5	33.5
5	49.3	54.9	54.5	49.4	49.5	49.2
6	27.1	24.8	24.0	28.1	28.1	27.6
7	36.8	38.2	37.3	36.9	36.1	36.3
8	145.9	145.7	146.5	145.2	145.2	146.5
9	49.9	52.4	47.7	51.6	51.7	46.1
10	38.6	53.0	52.3	51.0	51.1	50.4
11	23.6	22.9	36.6	23.7	23.7	38.1
12	24.2	24.5	193.0	25.7	37.0	194.6
13	124.5	124.6	127.8	125.0	125.1	128.0
14	110.7	110.8	108.6	111.0	110.0	107.8
15	142.9	142.7	144.2	142.6	142.6	144.1
16	138.8	138.8	147.1	138.8	138.9	147.3
17	109.1	108.0	107.6	108.2	108.3	108.6
18	23.3	27.1	26.8	23.7	23.7	23.6
19	176.2	176.4	176.4	76.4	173.0	76.6
20	73.0	205.1	204.9	172.9	76.4	173.4
OMe		51.4	51.4			

The measurements were made on a JEOL FX-100 spectrometer in $CDCl_3$ with TMS as an internal standard (δ=0.0ppm).

allocated to C-3 and C-7 respectively by comparison of the spectra of 1 and 8, since the chemical shift at C-7 was postulated not to change between 1 and 8. As for the absolute configuration of potamogetonin, the ORD curve of the synthetic 8 showed a positive plain curve, symmetrically opposite to the reported data for potamogetonin. Thus the structure of natural potamogetonin should be changed to 15,16-epoxy-8(17), 13(16),14-*ent*-labdatrien-20,19-olide, 10.



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4) 4 had been initially derived from sciadin by Sumimoto and now isolated from the seed by us.

5) This was prepared from lambertianic acid which had been isolated from the same seed.

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9) This compound has been recently isolated from *Cryptomeria japonica* by us; unpublished.

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