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Viburnols: Novel Triterpenoids with a Rearranged Dammarane Skeleton from *Viburnum dilatatum* 1)

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Abstract : Five novel triterpenoids, viburnols A(**1**), B(**2**), C(**3**), D(**4**) and E(**5**) , were isolated from the leaves of *Viburmun dilatatum* (Caprifoliaceae). The structures were determined by extensive spectroscopic studies. Viburnols A(**1**) and B(**2**) inhibited the growth of hypocotyls of lettuce seedlings. Copyright © 1996 Elsevier Science Ltd

The deciduous shrub *Viburnum dilatatum* is widely distributed in Japan and China.[2] The leaves have been utilized in traditional Chinese medicine (Chinese name, jia mi).[3] While Rice reported that *V.dilatatum* exhibited allelopathic activity, this plant does harm to adjacent vegetation.[4] In our previous paper,[5] we reported that the $CHCl_3$ extract of the leaves of *V.dilatatum* showed growth and germination inhibitory effects towards the seeds of head lettuce. From this extract, we isolated a new norisoprenoid along with seven known norisoprenoids and eight known phenolic compounds. In this communication we report the structures of five novel triterpenoids, viburnols A-E(**1-5**), from the remaining fractions of the same extract.[5]

Viburnol A(**1**)[6] was obtained as an amorphous powder, $[\alpha]_D$ +26.4°(c 1.0,$CHCl_3$). The molecular formula of **1** was assigned as $C_{30}H_{44}O_6$ on the basis of the MS and ^{13}C-NMR spectral data. The ^{13}C-NMR spectrum showed signals of 30 carbons including three oxygenated carbons[two methine(δ_C 79.3,82.9) and a quaternary(δ_C 74.4) carbon] and eight methyl groups. The spectral data of **1** revealed the presence of the partial structural units A[20-hydroxy-24-en-23-one type side chain [7] : 240nm(α,β-unsaturated ketone); 3507cm^{-1} (OH), 1674,1614 cm^{-1}(conjugated ketone); m/z 99, 83;δ_H 1.21(21-CH_3), 2.56(22-CH_2), 6.05(24-H), 1.92(26-CH_3), 2.17(27-CH_3) . δ_C 74.4(C-20), 26.3(C-21), 50.4(C-22), 202.5(C-23), 124.7(C-24), 158.1(C-25), 27.9(C-26), 21.1(C-27)] and B[two δ-lactones:1746cm^{-1};δ_H 4.41(s),4.52(ddd). δ_C 175.1,165.3, 82.9,79.3] (Fig.1). The molecular formula of **1** required 9 degrees of unsaturation. The α,β-unsaturated ketone of the side chain had 2 degrees of unsaturation, and therefore, **1** must have a five-ring system including two δ-lactone rings of the skeleton itself. The connectivities of the five rings, five methyl groups through the quaternary carbons, and the side chain were revealed by interpretation of the HMBC spectrum(Fig.2). On the basis of the above data, viburnol A(**1**) was suggested to be a highly oxygenated and rearranged dammarane-type triterpene having two δ-lactone rings. The relative stereochemistry of **1** was clarified by the NOE difference spectra(Fig.3). These NOE results suggested that the two δ-lactone rings should be fused *trans* at C-1 and C-10 positions. The presence of the 1β-oxygen atom produced γ-gauche shielding effect on the 19-methyl carbon(δ_C 10.6). Furthermore, as can be seen in Fig.3, NOE enhancements between 21-CH_3 and 12-Hβ

and 13-H, respectively, and between 22-CH_2 and 13-H were observed. Thus, the relative structure of viburnol A(**1**) including the side chain is clearly established as depicted in the formula. The relative structures of viburnols B(**2**),C(**3**),D(**4**) and E(**5**) were also elucidated on the basis of spectral data[6].

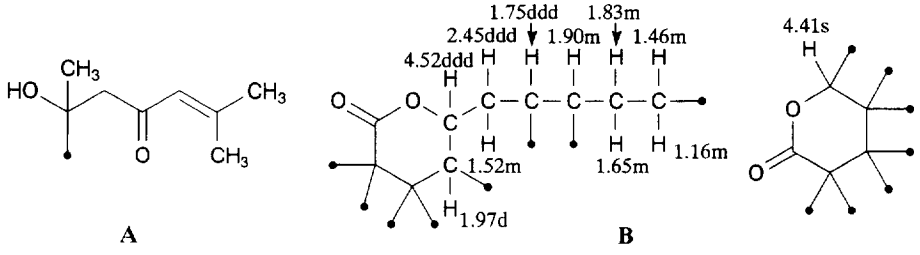


Fig.1 Partial Structural Units of 1

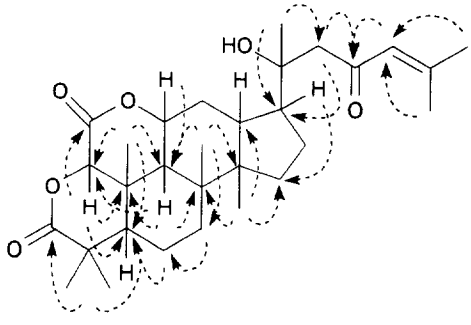


Fig.2 HMBC Correlations of 1

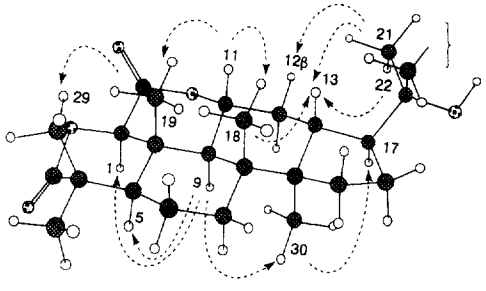
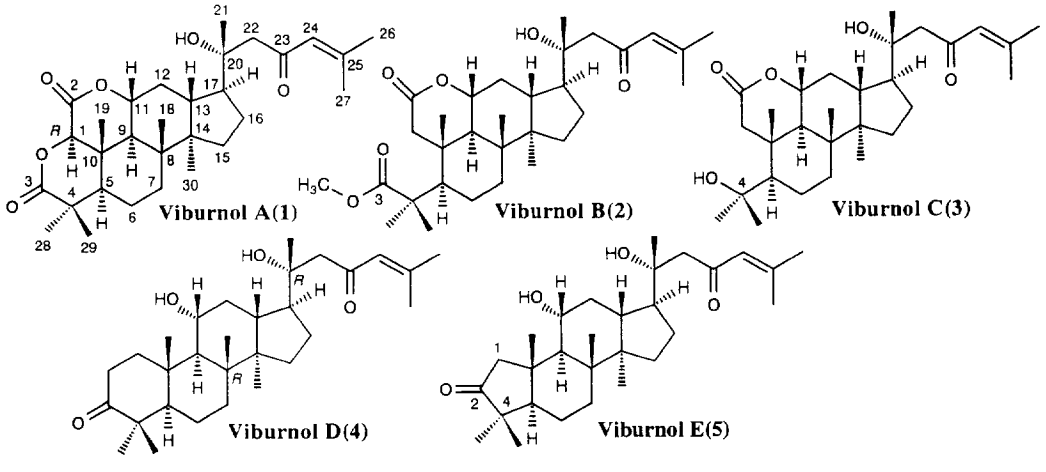


Fig.3 NOE Enhancements of 1

Viburnols A(**1**), B(**2**), C(**3**) and E(**5**) were presumably biosynthesized from viburnol D(**4**), so all the chiral centers of **1**(except C-1), **2**, **3** and **5** coincided with those of **4**. The CD spectrum of **4** showed a positive Cotton effect, $\triangle\varepsilon$ +1.06(289.5nm), suggesting that C-8 should have the *R*- configuration. Consequently, the configurations at C-1 of **1** and C-20 of **1**-**5** were determined as *R*, respectively. From these evidential details, the full structures of viburnols A-E(**1**-**5**) are established to be as shown.



Compounds **1-5** are a new dammarane-type triterpene, and compounds **1-3** are the first isolation of a new class of oxygenated and rearranged dammarane-type triterpene.

The inhibitory activities of viburnols A(**1**) and B(**2**) towards the germination of lettuce seedlings were not observed. Both compounds, however, inhibited the growth of hypocotyls of lettuce seedlings[at 55μg/cm^2, **1**(84.6%), **2**(79.5%) reductions in hypocotyl length growth are observed relative to the control].

Biosynthetic studies and investigation of the biological activities of viburnols A-E(**1-5**) and minor compounds will be undertaken in the near future.

Table 1. ^{13}C-NMR(67.8MHz,$CDCl_3$) Spectral Data for 1-5

C	1	2	3	4	5
1	82.9	48.3	50.5	42.0	58.6
2	165.3	170.0	171.1	34.2	225.7
3	175.1	179.1	-	218.7	-
4	41.7	45.4	75.5	47.7	43.9
5	53.2	55.3	57.9	55.2	59.8
6	18.6	19.9	22.2	19.6	17.9
7	34.4	34.9	34.6	35.1	35.3
8	39.2	39.4	39.3	40.6	40.1
9	47.3	47.3	47.2	54.7	54.7
10	35.7	38.1	37.6	38.2	41.2
11	79.3	77.2	77.1	71.2	69.7
12	33.8	35.0	35.1	39.7	38.3
13	41.2	40.7	40.7	41.2	41.1
14	49.7	50.1	50.1	49.97	50.1
15	30.7	30.6	30.7	30.7	30.7
16	25.1	25.0	25.0	25.0	25.2
17	49.1	49.3	49.3	50.1	50.1
18	15.8	15.3	15.2	16.2	16.9
19	10.6	17.9	17.4	16.8	17.8
20	74.4	74.4	74.4	74.8	74.8
21	26.3	25.8	25.7	26.5	26.4
22	50.4	51.1	51.2	50.0	50.1
23	202.5	202.6	202.6	202.8	202.8
24	124.7	124.7	124.4	124.9	124.8
25	158.1	157.8	157.8	157.6	157.6
26	27.9	27.9	27.9	27.8	27.9
27	21.1	21.0	21.0	21.0	21.0
28	29.8	27.9[a]	33.8[b]	27.5	27.6
29	23.3	22.7[a]	28.1[b]	20.7	20.9
30	16.3	16.4	16.3	16.1	16.6

Assignments were confirmed by ^{1}H-^{1}H and ^{13}C-^{1}H COSY and HMBC methods.

[a,b] Signals may be interchanged.

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6. **Viburnol A(1)**; ^{1}H-NMR(270MHz,$CDCl_3$):δ 6.05(1H,d,*J*=1.5Hz,24-H),4.52(1H,ddd,*J*=11.7, 11.5,4.8Hz,11-H),4.41(1H,s,1-H),2.56(2H,s,22-CH_2),2.45(1H,ddd,*J*=12.0,4.8,2.9Hz,12-H_β), 2.17(3H,s,27-CH_3), 1.97(1H,d,*J*=11.7Hz,9-H),1.92(3H,d,*J*=1.5Hz,26-CH_3),1.34(3H,s,28-CH_3), 1.27(3H,s,29-CH_3),1.21(3H,s,21-CH_3),1.15(3H,s,19-CH_3),1.10(3H,s,18-CH_3), 1.00(3H,s,30-CH_3). **Viburnol B(2**,$C_{31}H_{48}O_6$); [α]D +8.1°(*c* 1.6,$CHCl_3$). ^{1}H-NMR(270MHz,$CDCl_3$):δ 6.04 (1H,s,24-H),4.39(1H,ddd,*J*=11.9,10.7,5.0Hz,11-H),3.70(3H,s,$COOCH_3$),2.56(2H,s,22-CH_2),2.50 (1H,d,*J*=16.8Hz,1-H_β),2.38(1H,ddd,*J*=12.0,5.0,3.0Hz,12-H_β),2.28(1H,d,*J*=16.8Hz,1-H_α),2.17(3H, s,27-CH_3),1.92(3H,s,26-CH_3),1.78(1H,d,*J*=11.9Hz,9-H),1.24,1.22(each3H,s,28,29-CH_3),1.20(3H, s,21-CH_3),1.18(3H,s,19-CH_3),1.02(3H,18-CH_3),0.95(3H,s,30-CH_3). **Viburnol C(3**,$C_{29}H_{46}O_5$); [α]D +20.3°(*c* 2.9,$CHCl_3$). ^{1}H-NMR(270MHz,$CDCl_3$):δ 6.04(1H,s,24-H),4.42(1H,ddd,*J*=11.8, 11.2,5.0Hz,11-H),3.46(1H,d,*J*=18.2Hz,1-H_β),2.57(2H,s,22-CH_2),2.37(1H,ddd,*J*=12.2,5.0,3.0Hz, 12-H_β),2.28(1H,d,*J*=18.2Hz,1-H_α),2.17(3H,s,27-CH_3),1.92(3H,s,26-CH_3),1.76(1H,d,*J*=11.8Hz,9-H),1.31,1.27(each 3H,s,28,29-CH_3),1.26(3H,s,19-CH_3),1.21(3H,s,21-CH_3),1.04(3H,s,18-CH_3), 0.94(3H,s,30-CH_3). **Viburnol D(4**,$C_{30}H_{48}O_4$); [α]D +51.1°(*c* 1.0,$CHCl_3$). ^{1}H-NMR(270MHz, $CDCl_3$):δ 6.07(1H,s,24-H), 3.95(1H,ddd,*J*=10.7,10.6,5.0Hz,11-H), 2.66(1H,ddd,*J*=13.5,8.1,5.4Hz, 1-H_β), 2.57(2H,s,22-CH_2), 2.45(2H,m,2-CH_2),2.22(1H,m,12-H_β),2.17(3H,s,27-CH_3), 1.92(3H,s, 26-CH_3),1.54(1H,d,*J*=10.7Hz,9-H),1.21(3H,s,21-CH_3), 1.10(3H,s,28-CH_3), 1.07(6H,s,19,29-CH_3), 1.00(3H,s,18-CH_3), 0.92(3H,s,30-CH_3). CD(MeOH) $\Delta\varepsilon$ +1.06(289.5nm). **Viburnol E(5**,$C_{29}H_{46}O_4$); [α]D +76.4°(*c* 2.2,$CHCl_3$). ^{1}H-NMR(270MHz,CDCl3):δ 6.07(1H,s,24-H),3.90 (1H,ddd,*J*=10.9,10.6,5.3Hz,11-H),2.58(1H,d,*J*=16.5Hz,1-H_β),2.57(2H,s,22-CH_2),2.22(1H,m,12-H_β),2.17(3H,s,27-CH_3),2.15(1H,d,*J*=16.5Hz,1-H_α),1.91(3H,s,26-CH_3),1.68(1H,d,*J*=10.9Hz,9-H), 1.21(3H,s,21-CH_3), 1.006,0.997,0.989,0.975(15H,s,18,19,28,29,30-CH_3). CD(MeOH) $\Delta\varepsilon$ +2.79 (300.5nm).
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