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Viburnols: Six Novel Triterpenoids from *Viburnum dilatatum* [1]

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Abstract : Six novel triterpenoids, viburnols F(**1**), G(**2**), H(**3**), I(**4**), J(**5**) and K(**6**), were isolated from the leaves of *Viburnum dilatatum* (Caprifoliaceae). The structures were determined by extensive spectroscopic studies. **1**, **2** and **4** are the first isolation of a new rearranged dammarane-type triterpene.

We have recently reported the isolation of five new triterpenoids, viburnols A,B,C,D and E, from the $CHCl_3$ extract of the leaves of *Viburnum dilatatum*.[2] Among these triterpenoids, viburnols A and B inhibited the growth of hypocotyls in lettuce seedlings. In the present study, from the remaining fraction,[2,3] six novel triterpenoids with a rearranged dammarane skeleton, viburnols F(**1**), G(**2**), H(**3**), I(**4**), J(**5**) and K(**6**), were isolated. In this communication, we wish to report the structures of these new compounds.

Viburnol F(**1**)[4] was obtained as an amorphous powder, $[\alpha]_D$ +43.5°(*c* 0.3,$CHCl_3$). The molecular formula of **1** was assigned as $C_{31}H_{50}O_7$ on the basis of the MS and ^{13}C-NMR spectral data. The spectral data of **1** corresponding to rings B(except C-5,9 and 10), C and D and side chain are in fair agreement with those of viburnol E.[2] The major differences between **1** and viburnol E were the absence of a cyclic ketone(C-2) and a methylene(C-1) groups and the presence of two hydroxy-bearing carbons[a methine(δ_H 4.37, δ_C 82.5) and a quaternary(δ_C 85.5)] and a methoxycarbonyl group[δ_H 3.76, δ_C 174.9, 51.9] in ring A of **1**. These findings suggested that two hydroxyl groups are located at the C-1 and C-2 positions, respectively, and the methoxycarbonyl group is located at the hydroxy-bearing quaternary carbon(δ_C 85.5), in the five-membered A-ring of **1**. The placement of the methoxycarbonyl on C-2 was deduced from the HMBC spectrum. The carbon resonance at δ85.5 showed HMBC correlations with the methyl protons at δ1.05(28-CH_3) and 0.84(29-CH_3) which are also correlated to the quaternary carbon at δ46.7(C-4). On the other hand, the carbon resonance at δ82.5 showed HMBC correlation with the methyl protons at δ1.09(19-CH_3) which is also correlated to the quaternary carbon at δ46.0(C-10). The relative stereochemistry of **1** was clarified by the NOE difference spectra. The NOEs were observed between 1-H/19-CH_3(but not between 1-OH/19-CH_3) and 29-CH_3/2-$COOCH_3$ indicated that they were all on the same face(β) of the molecule, while interaction between 2-OH/28-CH_3 revealed that these were on the opposite face(α). Since the signal is due to the 9-H of **1** which was shifted to a lower field(Δ δ+0.46) than that of viburnol E, it is understood by the steric compression based on 1α-OH. All other HMBC and NOE correlations of **1** were consistent with those of viburnol E. On the basis of the above data, the relative structure of viburnol F(**1**) is clearly established as depicted in the formula. Viburnol F(**1**) is the first naturally-occurring dammarane-type triterpene having a five membered A-ring substituted at C-2.

Viburnol G(**2**)[4] was obtained as an amorphous powder, $[\alpha]_D$ +73.8°(*c* 0.4,$CHCl_3$). The molecular formula of **2** was assigned as $C_{31}H_{48}O_7$ on the basis of the MS and ^{13}C-NMR spectral data. From

comparison of the spectral data of **2** with those of viburnol E, it was deduced that **2** possesses the same rings B,C and D and side chain as in viburnol E. The major differences between **2** and viburnol E were the absence of a methylene(C-1) group and the presence of a hydroxy-bearing quaternary carbon[δ_C89.2] and a methoxycarbonyl group[δ_H3.76, δ_C172.4, 52.9] in ring A of **2**. These findings suggested that both tertiary alcohol and methoxycarbonyl groups are located at the C-1 position in the five- membered A-ring of **2**. This deduction was supported by HMBC spectrum. The carbon resonance at δ89.2 showed HMBC correlation with the methyl protons at δ1.02(19-CH_3) which is also correlated to the quaternary carbon at δ49.0(C-10). Furthermore, HMBC correlations were observed between the carbon resonance at δ217.5(C-3) and the proton resonances of 1-OH(δ5.64), 28-CH_3 and 29-CH_3(δ1.07,1.17). The stereochemistry of the hydroxy group at C-1 was determined as β on the NOE difference spectrum. Thus, the NOE was observed between 1-OH and 19-CH_3(β side). All other HMBC and NOE correlations of **2** were consistent with those of viburnol E. On the basis of the above data, the relative structure of viburnol G(**2**) is clearly established as depicted in the formula. Viburnol G(**2**) is the first naturally-occurring dammarane-type triterpene having a five membered A-ring substituted at C-1.

The relative structures of viburnols H(**3**), I(**4**), J(**5**) and K(**6**) were also elucidated on the basis of spectral data.[4] Viburnols H(**3**) and I(**4**) are the first naturally-occurring dammarane-type triterpene bearing a 2-keto and an α-ketoester groups, respectively. To our knowledge, viburnol K(**6**) is the first example of the ring A-tetranor(C-3,4,28 and 29)-triterpene isolated from the natural source.

Viburnols F(**1**), G(**2**), H(**3**), I(**4**),J(**5**) and K(**6**) were presumably biosynthesized from viburnol D(Scheme 1), so all the chiral centers of **1**(except C-1 and C-2), **2**(except C-1), **3**(except C-3), **4**(except C-1), **5** and **6** coincided with those of viburnol D, whose absolute configuration was elucidated by CD spectrum.[2] Consequently, the configurations at C-1 and C-2 of **1**, C-1 of **2**, C-3 of **3** and C-1 of **4** were determined as shown in Scheme 1. From these evidential details, the full structures of viburnols F-K(**1-6**) are established to be as shown.

Compounds **1-6** are a new dammarane-type triterpene, and compounds **1**,**2** and **4** are the first isolation of a new class of rearranged dammarane-type triterpene. Furthermore, the occurrence of compounds **1** and **2** gives important clues with regard to the biosynthesis of viburnol E.

It is expected that all viburnols(except viburnols D and H) are biosynthesized from the postulated intermediate(**7**; dammar-24-ene-2,3,23-trione-1α,11α,20α-triol), whose C-3 and C-4(route-A), C-2 and C-3(routes-B and C) and C-1 and C-2(route D) bonds cleavage followed recyclization to afford viburnols F(route-A),G(route-B),A(route-C) and I(route D), respectively.[5] This is the first report of the metabolic pathway of the dammarane-type triterpene.

Biosynthetic study of viburnols according to this scheme and minor compounds will be undertaken in the near future.

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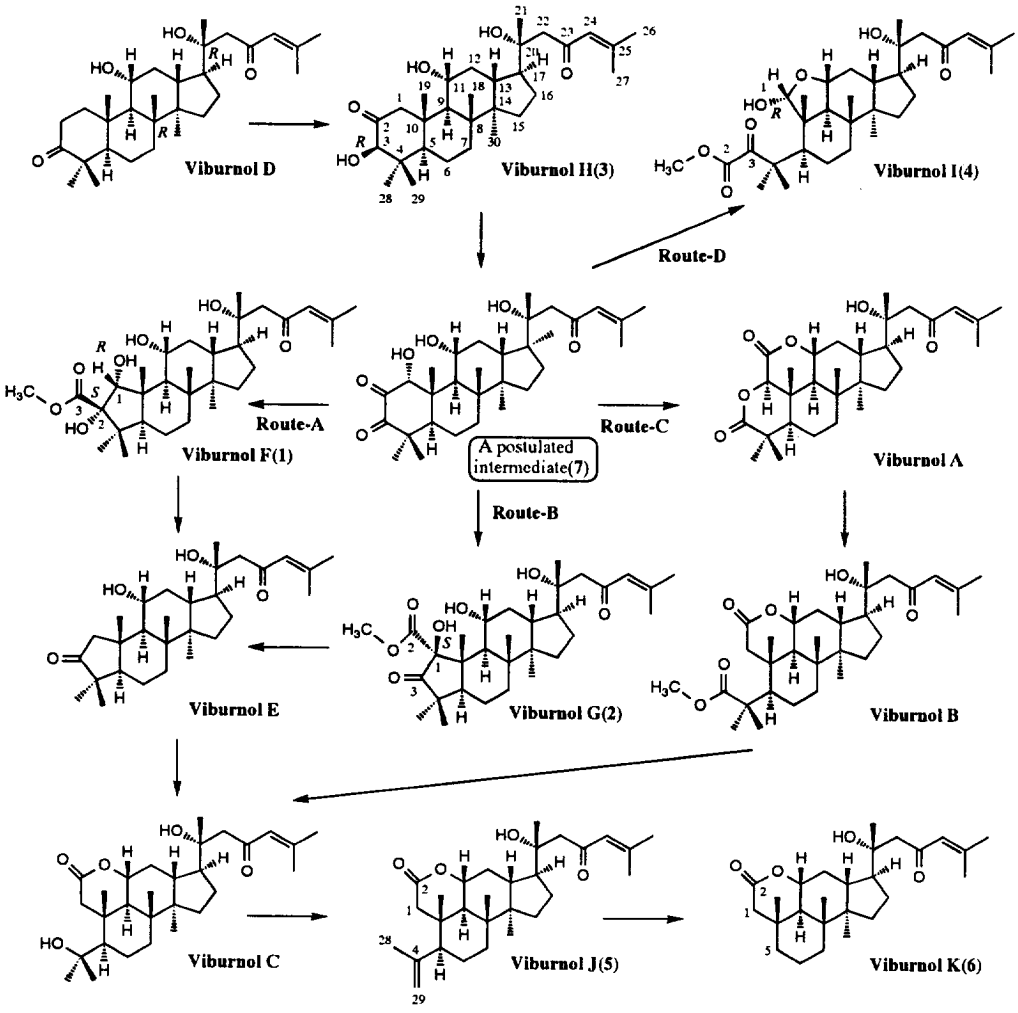

Scheme 1.

REFERENCES AND NOTES

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2. Machida, K. and Kikuchi, M. *Tetrahedron Lett.* **1996**, 37, 4157-4160.
3. Machida, K. and Kikuchi, M. *Phytochemistry*, **1996**, 41, 1333-1336.
4. **Viburnol F(1)**; EIMS *m/z* 516[M-H_2O]$^+$. FABMS *m/z* 535[M+H]$^+$. ^{1}H-NMR(270 MHz, $CDCl_3$):δ 6.07(1H, t, *J*= 1.2Hz, 24-H), 4.68(1H, br s, 1-OH), 4.40(1H, s, 20-OH), 4.37(1H, s, 1-H), 4.28(1H, s, 2-OH), 3.99(1H, ddd, *J*=11.2, 10.5, 5.0Hz, 11-H), 3.76(3H, s, $COOCH_3$), 2.61(1H, d, *J*=16.4Hz, 22-H_β), 2.54(1H, d, *J*=16.4Hz, 22-H_A), 2.44(1H, br s, 11-OH), 2.21(1H, m, 12-Hβ), 2.17(3H, d, *J*=1.2Hz, 27-CH_3), 2.14(1H, d, *J*=11.2Hz, 9-H), 1.91(3H, d, *J*=1.2Hz, 26-CH_3), 1.21(3H, s, 21-CH_3), 1.09(3H, s, 19-CH_3), 1.05(3H, s, 28-CH_3), 0.97(6H, s, 18, 30-CH_3), 0.84(3H, s, 29-

CH_3). ^{13}C-NMR(67.8 MHz,$CDCl_3$):δ 82.5(C-1), 85.5(C-2), 174.9(C-3), 46.7(C-4),55.9 (C-5), 17.9(C-6), 35.2(C-7), 41.2(C-8), 47.3(C-9), 46.0(C-10), 69.8(C-11), 38.2(C-12), 41.2(C-13), 50.2(C-14), 30.9(C-15), 25.2(C-16), 50.1(C-17), 16.8(C-18), 16.9(C-19), 74.9(C-20), 26.5(C-21), 50.0(C-22), 202.9(C-23), 124.9(C-24), 157.6(C-25), 27.9(C-26), 21.0(C-27), 25.3(C-28), 21.2(C-29), 16.7(C-30), 51.9($COOCH_3$).

Viburnol G(2); EIMS *m/z* 514[M-H_2O]$^+$. FABMS *m/z* 533[M+H]$^+$. ^{1}H-NMR(270 MHz,$CDCl_3$):δ 6.06(1H, d, *J*= 1.2Hz, 24-H), 5.64(1H, s, 1-OH), 4.37(1H, s, 20-OH), 3.82(1H, m, 11-H), 3.76(3H, s, $COOCH_3$), 3.34(1H, d, *J*= 8.9Hz, 11-OH), 2.57(2H, s, 22-CH_2), 2.32(1H, m, 12-Hβ), 2.17(3H, d, *J*=1.2Hz, 27-CH_3), 2.06(1H, d, *J*=10.6Hz, 9-H), 1.91(3H, d, *J*=1.2Hz, 26-CH_3), 1.20(3H, s, 21-CH_3), 1.17(3H, s, 28-CH_3), 1.07(3H, s, 29-CH_3), 1.02(6H, s,18, 19-CH_3), 0.94(3H, s, 30-CH_3). ^{13}C-NMR(67.8 MHz, $CDCl_3$):δ 89.2(C-1), 172.4(C-2), 217.5(C-3), 44.5(C-4), 51.6(C-5), 17.5(C-6), 35.0(C-7), 41.6(C-8), 49.1(C-9), 49.0(C-10), 69.5(C-11), 37.6(C-12), 41.4(C-13), 50.5(C-14), 30.8(C-15), 25.2(C-16), 50.0(C-17), 17.1(C-18), 14.5(C-19), 74.6(C-20), 26.0(C-21), 50.9(C-22), 202.8(C-23), 124.9(C-24), 57.8(C-25), 28.0(C-26), 21.2(C-27), 27.6(C-28), 22.3(C-29), 16.7(C-30), 52.9($COOCH_3$).

Viburnol H(3, $C_{30}H_{48}O_5$); [α]$_D$ +43.3°(*c* 0.7, $CDCl_3$). EIMS *m/z* 470[M-H_2O]$^+$. FABMS *m/z* 489[M+H]$^+$. ^{13}C-NMR(67.8 MHz,$CDCl_3$):δ 55.9(C-1), 212.3(C-2), 82.4(C-3), 45.3(C-4), 55.3(C-5), 18.3(C-6), 35.4(C-7), 41.0(C-8), 55.1(C-9), 44.8(C-10), 70.3(C-11), 39.7(C-12), 40.7(C-13), 50.1(C-14), 30.7(C-15), 25.0(C-16), 50.2(C-17), 16.3(C- 18), 17.7(C-19), 74.8(C-20), 26.5(C-21), 49.9(C-22), 202.8(C-23), 124.8(C-24), 157.6(C-25), 27.8(C-26), 21.0(C-27), 29.5(C-28), 16.5(C-29), 16.3(C-30).

Viburnol I(4, $C_{31}H_{48}O_7$); [α]$_D$ +20.0°(*c* 0.3, $CDCl_3$). IR ($CHCl_3$) cm^{-1}:1738, 1713(α-ketoester). EIMS *m/z* 514[M-H_2O]$^+$. FABMS *m/z* 533[M+H]$^+$. ^{1}H-NMR(270 MHz,$CDCl_3$):δ 6.04(1H, t, *J*=1.0Hz, 24-H), 4.99(1H, d, *J*= 2.5Hz, 1-H), 4.33(1H, s, 20-OH), 3.84(3H, s, $COOCH_3$), 3.73(1H, ddd, *J*=11.9, 11.1, 5.0Hz, 11-H),2.61(1H, d, *J*= 16.5Hz, 22-H$_B$), 2.53(1H, d, *J*=16.5Hz, 22-H$_A$), 2.36(1H, m, 12-Hβ), 2.34(1H, d, *J*=2.5Hz, 1-OH), 2.16(3H, d, *J*=1.0 Hz, 27-CH_3), 2.10(1H, d, *J*=11.9Hz, 9-H), 1.91(3H, d, *J*=1.0Hz, 26-CH_3), 1.37(3H, s, 29-CH_3), 1.25(3H, s, 28-CH_3), 1.20(3H, s, 21-CH_3), 1.07(3H, s, 19-CH_3), 0.97(3H, s, 18-CH_3), 0.96(3H, s, 30-CH_3). ^{13}C-NMR(67.8 MHz,$CDCl_3$) :δ 105.2(C-1), 164.9(C-2), 202.8(C-3), 50.3(C-4), 45.5(C-5), 22.7(C-6), 34.0(C-7), 38.2(C-8), 49.8(C-9), 47.5(C-10), 75.8(C-11), 34.5(C-12), 43.3(C-13), 50.2(C-14), 30.9(C-15), 26.0(C-16), 48.3(C-17), 15.3(C-18), 17.3(C-19), 74.8(C-20), 26.1(C-21), 50.6(C-22), 202.7(C-23), 124.8(C-24), 157.5(C-25), 27.9(C-26), 21.0(C-27), 20.5(C-28), 23.8(C-29), 16.0(C-30), 52.2($COOCH_3$).

Viburnol J(5, $C_{29}H_{44}O_4$); [α]$_D$ +45.5°(*c* 0.2, $CDCl_3$). EIMS *m/z* 438[M-H_2O]$^+$. FABMS *m/z* 457[M+H]$^+$. ^{13}C-NMR(67.8 MHz,$CDCl_3$):δ 48.9(C-1), 170.5(C-2), 144.5(C-4), 56.1(C-5), 23.7(C-6), 34.1(C-7), 39.1(C-8), 46.5(C-9), 35.7(C-10), 78.0(C-11), 34.7(C-12), 40.9(C-13), 50.1(C-14), 30.7(C-15), 25.0(C-16), 49.3(C-17), 15.2(C-18), 17.2(C-19), 74.4(C-20), 25.8(C-21), 51.0(C-22), 202.6(C-23), 124.7(C-24), 157.8(C-25), 27.9(C-26), 21.0(C-27), 22.9(C-28), 114.6(C-29), 16.4(C-30).

Viburnol K(6, $C_{26}H_{40}O_4$); [α]$_D$ +22.5°(*c* 0.4, $CDCl_3$). EIMS *m/z* 398[M-H_2O]$^+$. FABMS *m/z* 417[M+H]$^+$. ^{13}C-NMR(67.8 MHz,$CDCl_3$):δ 50.6(C-1), 170.4(C-2), 40.2(C-5), 18.1(C-6), 33.9(C-7), 39.2(C-8), 45.3(C-9), 32.1(C-10), 78.6(C-11), 34.7(C-12), 40.9(C-13), 50.0(C-14), 30.6(C-15), 25.0(C-16), 49.3(C-17), 15.0(C-18), 20.4(C-19), 74.4(C-20), 25.8(C-21), 51.0(C-22), 202.6(C-23), 124.7(C-24), 157.7(C-25), 27.9(C-26), 21.0(C-27), 16.3(C-30).

5. See for example: (a) Simpson, T. J.; Lunnon, M. W. and MacMillan, J. *J.Chem.Soc.*,Perkin I, **1979**, 931-934. (b) Loutsi, D. ; Sondengam, B. L. ; Martin, M. T. and Bodo, B. *Phytochemistry*, **1991**, 30, 2361-2364.

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