# Four New Insect Antifeedant *neo*-Clerodane Diterpenoids, Ajugacumbins A, B, C and D, from *Ajuga decumbens*

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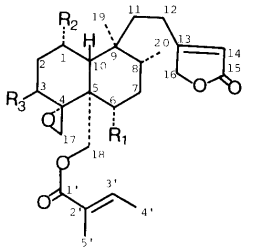
**From the ethanol extract of whole herbs of *Ajuga decumbens* (Labiatae), four new *neo*-clerodane diterpenoids, named ajugacumbins A, B, C and D (1—4), were isolated. The configuration of 1 was determined to be 6α-acetoxy-4,17-epoxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide by X-ray analysis. The other structures were also determined by spectroscopic analysis to be 4,17-epoxy-6α-hydroxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide (2), 1α,3β,6α-triacetoxy-4,17-epoxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide (3) and 6α-acetoxy-4,17-epoxy-3β-hydroxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide (4). These compounds displayed insect antifeedant activity.**

**Keywords** *Ajuga decumbens*; Labiatae; X-ray analysis; *neo*-clerodane diterpene; ajugacumbin A; ajugacumbin B; ajugacumbin C; ajugacumbin D; insect antifeedant activity

The whole herb of *Ajuga decumbens* THUNB. (Labiatae) ( 白毛夏枯草 , bái máo xià kū cǎo) ("kiranso" in Japanese) has been used for the treatment of sore throat, removing phlegm and alleviating fever as a folkloric crude drug. It tastes extremely bitter. The plant is distributed extensively in the southern area of China.[1] Up to the present, many compounds have been isolated from *Ajuga* species and their structures have been characterized; *neo*-clerodane diterpenes (ajugarins I—V,[2-4] and ajugamarins A1 and B1[5] C1, B2 and B3[6]), phytoecdysones (ajugalactone,[7] cyasterone,[8] and ajugasterone C[9]) and iridoid glycosides (decumbesides A—D),[10] with activities as insect antifeedants, insect molting inhibitors and bitter principles. From the ethanol extract of *A. decumbens*, four new *neo*-clerodane diterpenes, named ajugacumbins A, B, C and D, have been isolated. The present paper describes the structure elucidation of the new compounds.

Compound **1**, ajugacumbin A, was obtained as colorless crystals, mp 185—186 °C, $[\alpha]_D^{28} = +38.7°$ ($c=0.9$, $CHCl_3$). A signal, (M+1) $m/z$ 475, in the fast atom bombardment mass spectrum (FAB-MS) showed the molecular formula to be $C_{27}H_{38}O_7$. The proton nuclear magnetic resonance ($^1$H-NMR) spectrum exhibited signals [$\delta_H$: 5.81 (1H, t, $J_{14,16}=1.6$ Hz, H-14) and 4.72 (2H, d, $J_{16,14}=1.6$ Hz, H-16)], and in the carbon-13 NMR ($^{13}$C-NMR) spectrum four peaks $\delta_C$ 173.6 (s, C-13), 115.5 (d, C-14), 170.1 (s, C-15) and 73.0 (t, C-16) were also seen, which indicated the presence of a conjugated γ-lactone moiety bearing an α-H, as in ajugamarins.[5,6] Its ultraviolet (UV) [218 nm (log ε 4.2)] and infrared (IR) spectra (1779, 1744 and 1651 $cm^{-1}$) also supported the partial structure. The signals of an AB system at $\delta_H$ 2.96 (dd, $J=4.0$, 2.0 Hz, H-17, having W



**1**: $R_1$=OAc, $R_2$=$R_3$=H
**2**: $R_1$=OH, $R_2$=$R_3$=H
**3**: $R_1$=$R_2$=$R_3$=OAc
**4**: $R_1$=OAc, $R_2$=H, $R_3$=OH

Chart 1

TABLE I. $^1$H-NMR Spectral Data for Compounds **1**, **2**, **3** and **4** ($CDCl_3$, ppm; $J$ Values Are Shown in Hz)

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| $1_\beta$-H | *a)* | *a)* | 5.69, m, $W_{1/2}=15.0$ | *a)* |
| $2_\beta$-H | *a)* | *a)* | 2.71, ddd, $J_{2\beta,2\alpha}=15.0$, $J_{2\beta,3\alpha}=10.0$ $J_{2\beta,1\beta}=4.0$ | *a)* |
| $3_\alpha$-H | *a)* | *a)* | 5.85, dd, $J_{3\alpha,2\beta}=10.0$, $J_{3\alpha,2\alpha}=4.0$ | 4.79, dd, $J_{3\alpha,2\beta}=9.8$, $J_{3\alpha,2\alpha}=4.0$ |
| $6_\beta$-H | 4.68, dd, $J_{6\beta,7\alpha}=10.0$ $J_{6\beta,7\beta}=4.0$ | 3.57, dd, $J_{6\beta,7\alpha}=10.0$, $J_{6\beta,7\beta}=4.0$ | 4.67, dd, $J_{6\beta,7\alpha}=11.7$, $J_{6\beta,7\beta}=3.5$ | 4.75. dd, $J_{6\beta,7\alpha}=11.7$, $J_{6\beta,7\alpha}=4.4$ |
| 14-H | 5.81, t, $J_{14,16}=1.6$ | 5.84, t, $J_{14,16}=1.6$ | 5.88, t, $J_{14,16}=1.5$ | 5.94, t, $J_{14,16}=1.6$ |
| 16-$H_2$ | 4.72, d, $J_{16,14}=1.6$ | 4.75, d, $J_{16,14}=1.6$ | 4.79, dd, and 4.72, dd, $J_{16,16'}=17.6$, $J_{16,14}=1.5$ | 4.87, d, $J_{16,14}=1.6$ |
| 17-H | 2.96 and | 3.24 and | 3.00 and | 2.93 and |
| 17-H′ | 2.19, AB, $J_{17,17'}=4.0$ | 2.45, AB, $J_{17,17'}=4.0$ | 2.28, AB, $J_{17,17'}=4.0$ | 2.21, AB, $J_{17,17'}=3.1$ |
| 18-H | 4.84 and | 4.58, s | 4.98 and | 4.89 and |
| 18-H′ | 4.37, AB, $J_{18,18'}=12.0$ | 4.58, s | 4.43, AB, $J_{18,18'}=12.7$ | 4.42, AB, $J_{18,18'}=12.2$ |
| 19-$CH_3$ | 0.75, s | 0.77, s | 0.79, s | 0.78, s |
| 20-$CH_3$ | 0.79, d, $J=6.0$ | 0.86, d, $J=5.5$ | 0.85, d, $J=5.9$ | 0.82, d, $J=6.8$ |
| 3′-H | 7.03, q, $J=7.0$ | 6.98, q, $J=7.0$ | 6.95, q, $J=7.0$ | 7.07, q, $J=7.3$ |
| 4′-$CH_3$ | 1.76, d, $J=7.0$ | 1.79, d, $J=7.0$ | 1.80, d, $J=7.0$ | 1.80, d, $J=7.3$ |
| 5′-$CH_3$ | 1.84, s | 1.86, s | 1.88, s | 1.87, s |
| OAc | 1.83, s | | 1.96, s, 2.14, s, 2.18, s | 1.88, s |
| OH | | 3.44, br s | | 2.63, br s |

*a)* Means unassignable.

coupling with 3-axial proton) and 2.19 (d, $J=4.0$ Hz) were attributable to the exocyclic epoxide group. The signal patterns of the $^1$H- and $^{13}$C-NMR spectra were closely related to those of ajugarin I[2] except for the number of acetoxyl and tigloyloxyl groups. The number of them was confirmed by the following $^1$H- and $^{13}$C-NMR spectral data; $\delta_H$ 1.83 (3H, s), and $\delta_C$ 169.7 (s) and 21.1 (q) due to one acetyl group: $\delta_H$ 7.03 (1H, q, $J=7.0$ Hz, H-3′), 1.76 (3H, d, $J=7.0$ Hz, $CH_3$-4′) and 1.84 (3H, s, $CH_3$-5′), and $\delta_C$ 168.0 (s, C-1′), 128.6 (s, C-2′), 138.0 (d, C-3′), 14.5 (q, C-4′) and 12.0 (q, C-5′) due to one tigloyl group. Furthermore, the signals at $\delta_H$ 4.84 ($J=12.0$ Hz) and 4.37 ($J=12.0$ Hz) that appeared as an AB system were assigned to an α-oriented methylene at C-18, and the signals at $\delta_H$ 4.68 (dd, $J_{6\beta,7\alpha}=10.0$ and $J_{6\beta,7\beta}=4.0$ Hz) were assignable to H-6β after comparison with those of ajugarin I.[2] These lower chemical shifts implied the presence of oxo-substituents at C-5 and C-6. But the locations of the substituents (acetyl or tigloyl) remained ambiguous (C-6α or C-18).

Table II. $^{13}$C-NMR (DEPT) Spectral Data for Compounds **1**, **2**, **3** and **4** ($CDCl_3$, ppm)

| Carbon No. | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| 1 | 22.0 (t) | 22.0 (t) | 70.1 (d) | 21.6 (t) |
| 2 | 21.0 (t) | 20.7 (t) | 40.3 (t) | 24.7 (t) |
| 3 | 25.1 (t) | 25.0 (t) | 66.7 (d) | 63.2 (d) |
| 4 | 65.0 (s) | 67.0 (s) | 64.2 (s) | 65.2 (s) |
| 5 | 45.3 (s) | 45.3 (s) | 45.9 (s) | 45.6 (s) |
| 6 | 72.0 (d) | 73.7 (d) | 71.3 (d) | 72.2 (d) |
| 7 | 32.9 (t) | 31.8 (t) | 30.3 (t) | 32.7 (t) |
| 8 | 34.7 (d) | 34.7 (d) | 35.0 (d) | 35.3 (d) |
| 9 | 38.3 (s) | 38.5 (s) | 38.9 (s) | 39.4 (s) |
| 10 | 48.1 (d) | 48.6 (d) | 50.9 (d) | 48.9 (d) |
| 11 | 32.5 (t) | 33.6 (t) | 32.0 (t) | 32.9 (t) |
| 12 | 34.7 (t) | 34.5 (t) | 32.4 (t) | 33.1 (t) |
| 13 | 173.6 (s) | 173.7 (s) | 172.3 (s) | 173.6 (s) |
| 14 | 115.5 (d) | 115.2 (d) | 115.8 (d) | 114.6 (d) |
| 15 | 170.1 (s) | 169.1 (s) | 168.4 (s) | 168.4 (s) |
| 16 | 73.0 (t) | 72.9 (t) | 70.6 (t) | 70.7 (t) |
| 17 | 48.1 (t) | 48.6 (t) | 48.4 (t) | 48.1 (t) |
| 18 | 61.5 (t) | 61.8 (t) | 61.4 (t) | 61.5 (t) |
| 19 | 17.4 (q) | 17.5 (q) | 16.8 (q) | 17.3 (q) |
| 20 | 15.3 (q) | 15.4 (q) | 15.3 (q) | 15.5 (q) |
| 1′ | 168.0 (s) | 168.0 (s) | 168.4 (s) | 169.3 (s) |
| 2′ | 128.6 (s) | 128.3 (s) | 129.3 (s) | 128.7 (s) |
| 3′ | 138.0 (d) | 137.8 (d) | 138.2 (d) | 138.1 (d) |
| 4′ | 14.5 (q) | 14.5 (q) | 14.5 (q) | 14.6 (q) |
| 5′ | 12.0 (q) | 11.9 (q) | 12.2 (q) | 12.0 (q) |
| OAc | 21.1 (q) | | 21.1 (q) | 21.2 (q) |
| | | | 21.0 (q) | |
| | | | 21.0 (q) | |
| CO | 169.7 (s) | | 169.4 (s) | 170.4 (s) |
| | | | 169.8 (s) | |
| | | | 170.2 (s) | |

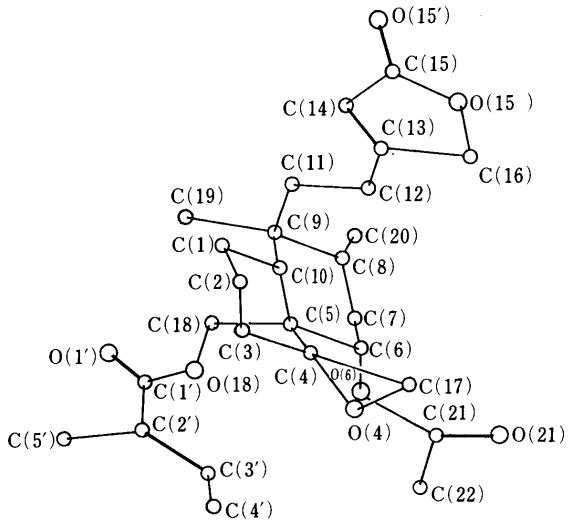



Fig. 1. Computer-Generated Structural Drawing of Ajugacumbin A (**1**)

Table III. Atomic Coordinates ($\times 10^4$) and Isotropic Thermal Parameters (Å $2\times 10^3$) for **1**

| | X | Y | Z | U |
|---|---|---|---|---|
| C(1) | 10819 (5) | 4231 (4) | 2008 (4) | 55 (2)[a] |
| C(2) | 11701 (7) | 4503 (5) | 1113 (5) | 73 (2)[a] |
| (C3) | 12444 (5) | 5626 (5) | 1322 (4) | 67 (2)[a] |
| C(4) | 11306 (5) | 6471 (4) | 1427 (4) | 53 (2)[a] |
| C(5) | 10555 (5) | 6279 (4) | 2437 (4) | 40 (1)[a] |
| C(6) | 9386 (4) | 7165 (4) | 2528 (4) | 47 (1)[a] |
| C(7) | 8411 | 6882 | 3353 | 55[a] |
| C(8) | 7595 (5) | 5773 (4) | 3036 (4) | 48 (2)[a] |
| C(9) | 8652 (5) | 4806 (4) | 2963 (4) | 42 (1)[a] |
| C(10) | 9734 (5) | 5145 (4) | 2178 (4) | 40 (1)[a] |
| C(11) | 7721 (5) | 3786 (4) | 2439 (4) | 45 (1)[a] |
| C(12) | 6888 (5) | 3878 (4) | 1209 (4) | 56 (2)[a] |
| C(13) | 5726 | 3019 | 857 | 48[a] |
| C(14) | 5258 | 2228 | 1446 | 68[a] |
| C(15) | 4087 | 1612 | 706 | 76[a] |
| C(16) | 4880 | 2945 | −326 | 65[a] |
| C(17) | 10509 | 6981 | 367 | 73[a] |
| C(18) | 11726 | 6249 | 3556 | 51[a] |
| C(19) | 9463 (5) | 4440 (5) | 4156 (4) | 53 (2)[a] |
| C(20) | 6525 (7) | 5578 (6) | 3841 (7) | 82 (3)[a] |
| C(21) | 9631 | 9122 | 2339 | 56[a] |
| C(22) | 10676 (8) | 10072 (5) | 2702 (5) | 87 (3)[a] |
| C(1′) | 13670 | 7400 | 4528 | 51[a] |
| C(2′) | 14816 | 8203 | 4401 | 56[a] |
| C(3′) | 14727 | 8774 | 3448 | 70[a] |
| C(4′) | 15778 (9) | 9658 (7) | 3254 (8) | 110 (3)[a] |
| C(5′) | 16034 (6) | 8322 (6) | 5450 (5) | 84 (2)[a] |
| O(4) | 11643 | 7583 | 1157 | 67[a] |
| O(6) | 10152 | 8196 | 2899 | 53[a] |
| O(15′) | 3305 | 852 | 904 | 109[a] |
| O(15) | 3875 | 2040 | −339 | 80[a] |
| O(18) | 12878 | 7030 | 3506 | 49[a] |
| O(20) | 13445 | 7058 | 5417 | 76[a] |
| O(21) | 8512 | 9150 | 1621 | 77[a] |

*a*) Equivalent isotropic $U$ defined as one-third of the trace of the orthogonalized $U_{ij}$ tensor.

Table IV. Bond Lengths (Å) in **1**

| | | | |
|---|---|---|---|
| C(1)–C(2) | 1.514 (8) | C(2)–C(3) | 1.522 (8) |
| C(3)–C(4) | 1.489 (8) | C(4)–O(4) | 1.437 (5) |
| C(4)–C(17) | 1.469 (4) | C(5)–C(6) | 1.540 (6) |
| C(5)–C(4) | 1.536 (7) | C(5)–C(18) | 1.540 (4) |
| C(6)–O(6) | 1.459 (4) | C(7)–C(6) | 1.510 (5) |
| C(7)–C(8) | 1.550 (5) | C(8)–C(9) | 1.539 (7) |
| C(8)–C(20) | 1.537 (10) | C(9)–C(19) | 1.539 (6) |
| C(9)–C(10) | 1.563 (7) | C(10)–C(5) | 1.569 (6) |
| C(9)–C(11) | 1.561 (6) | C(12)–C(13) | 1.491 (5) |
| C(10)–C(1) | 1.535 (7) | C(13)–C(16) | 1.477 (1) |
| C(11)–C(12) | 1.523 (6) | C(15)–O(15) | 1.336 (1) |
| C(13)–C(14) | 1.317 (1) | C(16)–O(15) | 1.434 (1) |
| C(14)–C(15) | 1.454 (1) | C(17)–O(4) | 1.454 (1) |
| C(15)–O(15′) | 1.224 (1) | C(21)–C(22) | 1.506 (7) |
| C(18)–O(18) | 1.433 (1) | C(21)–O(21) | 1.200 (1) |
| C(21)–O(6) | 1.346 (1) | C(1′)–O(18) | 1.368 (1) |
| C(1′)–C(2′) | 1.467 (1) | C(2′)–C(5′) | 1.511 (5) |
| C(1′)–O(1′) | 1.205 (1) | C(3′)–C(4′) | 1.485 (8) |
| C(2′)–C(3′) | 1.328 (1) | | |

TABLE V. Bond Angles (°) in **1**

| | | | |
|---|---|---|---|
| C(10)–C(1)–C(2) | 113.4 (4) | C(1)–C(2)–C(3) | 111.5 (5) |
| C(2)–C(3)–C(4) | 109.3 (4) | C(5)–C(4)–C(3) | 113.8 (4) |
| C(5)–C(4)–C(17) | 121.7 (4) | C(3)–C(4)–C(17) | 116.7 (4) |
| C(5)–C(4)–O(4) | 118.4 (4) | C(3)–C(4)–O(4) | 115.9 (4) |
| C(17)–C(4)–O(4) | 60.0 (2) | C(4)–O(4)–C(17) | 61.1 (2) |
| C(10)–C(5)–C(4) | 104.6 (4) | C(10)–C(5)–C(6) | 108.1 (3) |
| C(10)–C(5)–C(18) | 111.9 (3) | C(6)–C(5)–C(4) | 112.8 (4) |
| C(4)–C(5)–C(18) | 110.2 (3) | C(6)–C(5)–C(18) | 109.1 (3) |
| C(7)–C(6)–O(6) | 108.0 (3) | C(7)–C(6)–C(5) | 114.1 (3) |
| C(8)–C(7)–C(6) | 111.1 (3) | C(5)–C(6)–O(6) | 108.6 (3) |
| C(7)–C(8)–C(20) | 108.7 (4) | C(6)–O(6)–C(21) | 117.6 (2) |
| C(8)–C(9)–C(10) | 108.9 (4) | C(7)–C(8)–C(9) | 113.3 (3) |
| C(10)–C(9)–C(19) | 113.1 (4) | C(9)–C(8)–C(20) | 114.5 (5) |
| C(10)–C(9)–C(11) | 109.3 (4) | C(8)–C(9)–C(19) | 110.9 (4) |
| C(9)–C(10)–C(5) | 116.8 (4) | C(8)–C(9)–C(11) | 109.0 (3) |
| C(5)–C(10)–C(1) | 111.2 (4) | C(19)–C(9)–C(11) | 105.4 (4) |
| C(9)–C(11)–C(16) | 117.2 (4) | C(9)–C(10)–C(1) | 113.8 (4) |
| C(11)–C(12)–C(13) | 114.3 (4) | C(12)–C(13)–C(14) | 130.7 (2) |
| C(12)–C(13)–C(16) | 121.3 (2) | C(14)–C(13)–C(16) | 107.9 (1) |
| C(13)–C(14)–C(15) | 109.2 (1) | C(14)–C(15)–O(15′) | 108.7 (1) |
| C(14)–C(15)–O(15′) | 131.2 (1) | O(15′)–C(15)–O(15) | 119.9 (1) |
| C(13)–C(16)–O(15) | 105.5 (1) | C(15)–O(15)–C(16) | 108.6 (1) |
| C(4)–C(17)–C(4) | 58.9 (2) | C(5)–C(18)–O(18) | 109.8 (2) |
| C(22)–C(21)–O(6) | 126.0 (2) | C(22)–C(21)–O(6) | 110.7 (2) |
| C(2′)–C(1′)–O(18) | 112.6 (1) | O(6)–C(21)–O(21) | 123.2 (1) |
| O(18)–C(1′)–O(1′) | 121.7 (1) | C(2′)–C(1′)–O(1′) | 125.6 (1) |
| C(1′)–C(2′)–C(3′) | 121.3 (1) | C(1′)–C(2′)–C(5′) | 113.7 (3) |
| C(2′)–C(3′)–C(4′) | 125.7 (3) | C(5′)–C(2′)–C(3′) | 125.0 (3) |

TABLE VI. Anisotropic Thermal Parameters (Å2 × $10^3$) for **1**

| | *U*11 | *U*22 | *U*33 | *U*23 | *U*13 | *U*12 |
|---|---|---|---|---|---|---|
| C(1) | 50 (3) | 58 (3) | 54 (3) | −5 (2) | 5 (2) | 2 (2) |
| C(2) | 73 (3) | 78 (4) | 75 (4) | −24 (3) | 29 (3) | −5 (3) |
| C(3) | 53 (3) | 93 (4) | 61 (3) | −5 (3) | 28 (2) | −1 (3) |
| C(4) | 53 (3) | 61 (3) | 44 (2) | −2 (2) | 10 (2) | −12 (2) |
| C(5) | 34 (2) | 47 (3) | 35 (2) | 1 (2) | −1 (2) | −5 (2) |
| C(6) | 48 (2) | 43 (2) | 44 (2) | −1 (2) | −3 (2) | −6 (2) |
| C(7) | 55 | 52 | 60 | −2 | 19 | −7 |
| C(8) | 38 (2) | 48 (3) | 57 (3) | −2 (2) | 6 (2) | −5 (2) |
| C(9) | 38 (2) | 49 (3) | 34 (2) | 3 (2) | 0 (2) | −5 (2) |
| C(10) | 34 (2) | 45 (3) | 37 (2) | −2 (2) | −2 (2) | −2 (2) |
| C(11) | 44 (2) | 45 (2) | 42 (2) | 6 (2) | −2 (2) | −4 (2) |
| C(12) | 56 (3) | 59 (3) | 47 (2) | 6 (2) | −5 (2) | −19 (2) |
| C(13) | 45 | 53 | 43 | −5 | 3 | −2 |
| C(14) | 73 | 72 | 52 | −9 | −1 | −22 |
| C(15) | 70 | 77 | 78 | −14 | 9 | −33 |
| C(16) | 60 | 80 | 49 | −1 | −4 | −8 |
| C(17) | 91 | 86 | 41 | 5 | 7 | −21 |
| C(18) | 42 | 62 | 42 | 5 | −6 | −11 |
| C(19) | 53 (3) | 64 (3) | 36 (2) | 6 (2) | −2 (2) | −5 (3) |
| C(20) | 64 (4) | 78 (4) | 118 (6) | −4 (4) | 49 (4) | −3 (4) |
| C(21) | 73 | 49 | 49 | 1 | 15 | −3 |
| C(22) | 128 (6) | 58 (3) | 76 (4) | 1 (3) | 25 (4) | −25 (4) |
| C(1′) | 44 | 55 | 49 | −9 | −4 | 2 |
| C(2′) | 44 | 59 | 62 | −18 | 3 | −2 |
| C(3′) | 65 | 56 | 89 | −15 | 13 | −15 |
| C(4′) | 118 (5) | 80 (5) | 136 (6) | −2 (4) | 35 (5) | −35 (4) |
| C(5′) | 54 (3) | 99 (5) | 89 (4) | −36 (4) | −6 (3) | −18 (3) |
| O(4) | 69 | 71 | 62 | 2 | 15 | −20 |
| O(6) | 58 | 44 | 52 | −3 | 2 | −8 |
| O(15′) | 111 | 106 | 100 | −8 | 0 | −50 |
| O(15) | 68 | 92 | 70 | −22 | −9 | −23 |
| O(18) | 39 | 61 | 44 | −5 | 0 | −13 |
| O(20) | 75 | 98 | 49 | −2 | −1 | −19 |
| O(21) | 87 | 63 | 74 | 17 | 0 | 6 |

The anisotropic temperature factor exponent takes the form: $-2-2(h2a^{*}2U11+\cdots+2hka^{*}b^{*}U12)$.

For the confirmation of the structure (**1**), including its configuration, **1** was subjected to X-ray analysis. The crystals for the X-ray crystallographic study were recrystallized from MeOH. The results of X-ray analysis led to the conclusion that the acetoxyl and the tigloyloxyl groups are located at C-6α and C-18, respectively, the configurations of H-10, $CH_3$-19 and $CH_3$-20 are β, α and α, respectively, and also that the A and B rings are in chair forms. The structure of ajugacumbin A could therefore be formulated as 6α-acetoxy-4,17-epoxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide (**1**). A computer-generated drawing of **1** and related data are shown in Fig. 1 and Tables III—VII.

Compound **2**, ajugacumbin B, was obtained as colorless crystals, mp 194—195 °C, $[\alpha]_D^{28}=+40.5°$ ($c=0.74$, $CHCl_3$) and showed [M+1] at *m/z* 433 in the FAB-MS, which corresponds to $C_{25}H_{36}O_6$. The $^1$H- and $^{13}$C-NMR spectra of **2** were fundamentally identical with those of **1** except for the presence of a hydroxyl group in place of the acetyl group. The signal at $\delta_H$ 3.44 (1H) (disappeared with $D_2O$) was assignable to a hydroxyl group. Barton *et al.*[11] reported that the signal of the geminal proton (H-6) appeared as a double-doublet at $\delta_H$ 3.7—3.8 and that of H-18 appeared a singlet at 4.4 when the C-6α of the clerodane diterpene skeleton was substituted with a hydroxyl group,

TABLE VII. H-Atom Coordinates (× $10^4$) and Isotropic Thermal Parameters (Å 2 × $10^3$) for **1**

| | *X* | *Y* | *Z* | *U* |
|---|---|---|---|---|
| H(1a) | 10265 | 3567 | 1790 | 69 |
| H(1b) | 11502 | 4115 | 2718 | 69 |
| H(2a) | 11044 | 4502 | 379 | 84 |
| H(2b) | 12453 | 3951 | 1130 | 84 |
| H(3a) | 12897 | 5814 | 697 | 73 |
| H(3b) | 13189 | 5605 | 2011 | 73 |
| H(6) | 8742 | 7220 | 1792 | 50 |
| H(7a) | 9018 | 6827 | 4103 | 66 |
| H(7b) | 7687 | 7454 | 3339 | 66 |
| H(8) | 7016 | 5814 | 2275 | 53 |
| H(10) | 9049 | 5253 | 1468 | 47 |
| H(11a) | 7004 | 3639 | 2897 | 57 |
| H(11b) | 8392 | 3174 | 2486 | 57 |
| H(12a) | 7596 | 3821 | 727 | 65 |
| H(12b) | 6417 | 4588 | 1107 | 65 |
| H(14) | 5631 | 2081 | 2238 | 81 |
| H(16a) | 5536 | 2806 | −835 | 74 |
| H(16b) | 4341 | 3615 | −543 | 74 |
| H(17a) | 9353 | 7297 | 295 | 104 (16) |
| H(17b) | 10732 | 6779 | −303 | 125 (18) |
| H(18a) | 12147 | 5523 | 3664 | 62 |
| H(18b) | 11268 | 6429 | 4180 | 62 |
| H(19a) | 9979 | 5048 | 4571 | 63 |
| H(19b) | 10162 | 3837 | 4075 | 63 |
| H(19c) | 8750 | 4151 | 4559 | 63 |
| H(20a) | 6019 | 4885 | 3684 | 102 |
| H(20b) | 5811 | 6165 | 3743 | 102 |
| H(20c) | 7085 | 5579 | 4609 | 102 |
| H(22a) | 10107 | 10713 | 2418 | 100 |
| H(22b) | 11530 | 10023 | 2362 | 100 |
| H(22c) | 10993 | 10126 | 3512 | 100 |
| H(3′) | 13897 | 8620 | 2839 | 82 |
| H(4′a) | 15418 | 9902 | 2486 | 121 |
| H(4′b) | 16760 | 9362 | 3327 | 121 |
| H(4′c) | 15804 | 10271 | 3763 | 121 |
| H(5′a) | 16786 | 8809 | 5290 | 98 |
| H(5′b) | 16449 | 7601 | 5624 | 98 |
| H(5′c) | 15668 | 8597 | 6088 | 98 |

whereas the signal of geminal proton (H-6) moved to lower field at $\delta_H$ 4.5 and that of H-18 appeared as a double-doublet at 4.40 and 4.82 when an acetyl group was placed at the same position. The $^1$H-NMR spectrum of **2** exhibited signals attributable to H-6$\beta$ at $\delta_H$ 3.57 (dd, $J_{6\beta,7\alpha}=10.0$ Hz, $J_{6\beta,7\beta}=4.0$ Hz) as a double-doublet and to H-18 at 4.58 as a singlet, indicating the presence of a hydroxyl group at H-6$\beta$. Therefore, the structure of ajugacumbin B could be characterized as 4,17-epoxy-6$\alpha$-hydroxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide (**2**).

Compound **3**, ajugacumbin C, was obtained as an amorphous powder, $[\alpha]_D^{28}=+57.7°$ ($c=0.78$, $CHCl_3$). The electron impact mass spectrum (EI-MS) showed $[M^+-1]$ at $m/z$ 589, which corresponds to the molecular formula $C_{31}H_{42}O_{11}$. Except for the presence of three acetyl groups ($\delta_H$ 1.96, 2.14 and 2.18), the spectral data of **3** were similar to those of **1**. In the $^1$H-NMR spectrum, the signals at $\delta_H$ 4.67, 5.69 and 5.85 were assigned to the geminal protons of three acetyl groups. By comparison of the $^1$H-NMR spectrum with that of ajugarin I,[2] the signal at $\delta_H$ 4.67 could be assigned to H-6, which indicated that one of the acetyl groups was located at C-6$\alpha$. The $^1$H–$^1$H chemical shift correlation spectroscopy (COSY) spectrum showed the presence of coupling relations among H-1, H-2 and H-3. A double-doublet at $\delta_H$ 5.85 ($J_{3\alpha,2\beta}=10.0$ Hz, $J_{3\alpha,2\alpha}=4.0$ Hz) indicated that the position of a second acetyl group was at C-3$\beta$. The signals of $\delta_H$ 2.71 (ddd, $J_{2\beta,2\alpha}=15.0$ Hz, $J_{2\beta,3\alpha}=10.0$ Hz, and $J_{2\beta,1\beta}=4.0$ Hz) and 5.69 (m, $W_{1/2}=15.0$ Hz) were assignable to H-2$\beta$ and H-1$\alpha$. The coupling constants and the chemical shifts revealed a third acetyl group to be at C-1$\alpha$. Thus, ajugacumbin C was formulated as 1$\alpha$,3$\beta$,6$\alpha$-triacetoxy-3,4,17-epoxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide.

Compound **4**, ajugacumbin D, was obtained as colorless crystals, mp 183—184 °C, $[\alpha]_D^{28}=+33.9°$ ($c=1.2$, $CHCl_3$). From the FAB-MS, the molecular formula could be estimated as $C_{27}H_{38}O_8$. Except for the presence of a hydroxyl group, the spectral data of **4** showed the same groups as in **1**. Comparison of the $^{13}$C-NMR spectra of **4** and **1** showed that **4** lacks the signal at $\delta_C$ 25.10 in **1**, but exhibits a new signal at 65.24. The $^1$H-NMR spectrum also exhibited a new signal at $\delta_H$ 4.79 (dd, $J_{3\alpha,2\beta}=9.8$ Hz, $J_{3\alpha,2\alpha}=4.0$ Hz). The results indicated the existence of an oxo-substituent at C-3$\beta$ in **4**. AB signals at $\delta_H$ 4.42 (d) and 4.89 (d) due to H-18 and a double-doublet at 4.75 ($J_{6\beta,7\alpha}=11.7$ Hz, $J_{6\beta,7\beta}=4.4$ Hz) revealed that an acetyl group was located at C-6$\beta$ and a hydroxyl group may be located at C-3$\beta$. Therefore the structure of ajugacumbin D was concluded to be 6$\alpha$-acetoxy-4,17-epoxy-3$\beta$-hydroxy-18-tigloyloxy-*neo*-cleroda-13-en-15,16-olide (**4**).

Compounds **1**—**3** displayed insect antifeedant activity as detected by the host-plant leaf disc method using *Boehmeria nivea* with the larvae of *Pareba vesta* Fabricius. The results are shown in Table VIII.

TABLE VIII. Insect Antifeedant Activity of Compounds **1**—**3**

| Compound | Lowest effective concentration (ppm) |
|---|---|
| **1** | 50 |
| **2** | 200 |
| **3** | 200 |

## Experimental

**Plant Material** *Ajuga decumbens* THUNB. was collected in Jiangxi province, China, and a voucher specimen was deposited in the Herbarium of China Pharmaceutical University.

**Extraction and Isolation** The whole plants (8 kg; dried naturally, and powdered) of *A. decumbens* were extracted with ethanol three times. The extract was concentrated, and a certain volume of water was added and agitated thoroughly to form a suspension, which was extracted with chloroform. the concentrated $CHCl_3$ fraction (100 g) was subjected to column chromatography on silica gel eluted with a solution of ethyl acetate in petroleum ether. The crude crystals obtained were recrystallized from ethyl acetate–cyclohexane to give pure compounds **1** (3.2 g), **2** (12 mg), **3** (40 mg) and **4** (35 mg).

**Compound 1 (Ajugacumbin A)** Colorless crystals, mp 185—186 °C (EtOAc–cyclohexane), $[\alpha]_D^{28}$ +38.7° ($c=0.9$, $CHCl_3$), MW 474 (FAB-MS 475 $[M+1]$) for $C_{27}H_{38}O_7$. UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 218 (4.2). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 2935, 1779, 1744, 1705, 1651, 1373, 1276, 1246, 1141, 1129, 1022, 1007, 951, 887, 742. The $^1$H- and $^{13}$C-NMR data are shown in Tables I and II. EI-MS $m/z$ (rel. int.): $M^+$ (absent), 431 (0.9), 361 (2.8), 319 (16.1), 301 (4.6), 175 (6.5), 111 (4.7), 105 (5.6), 91 (6.5), 83 (100), 55 (46.8), 43 (27.0).

**Crystallographic Data** Monoclinic system, space group $P2_1$, cell dimensions are $a=9.207$ (2), $b=12.131$ (4), $c=12.030$ (3) Å, $\beta=102.01$ (2), $V=1314.37$ Å$^3$, $Z=2$. Intensity data were collected in the range of $1<\theta<57$ by an R3m/E four-circle diffractometer. Cu$K_\alpha$ radiation (graphite-monochromated), and 1994 independent reflections were recorded; 1754 with $I\geqslant 3(I)$ were considered as observed. The molecular structure was solved by direct methods. Thirty-one atoms were located from the $E$ map. Least-squares refinement and Fourier synthesis gave the coordinates of all carbon and oxygen atoms. Molecular formula $C_{27}H_{38}O_7$.

**Compound 2 (Ajugacumbin B)** Colorless crystals, mp 194—195 °C (EtOAc–cyclohexane), $[\alpha]_D^{28}$ +40.5° ($c=0.74$, $CHCl_3$), MW 432 (FAB-MS; 433 $[M+1]$) for $C_{25}H_{36}O_6$. UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 217 (4.24). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3476, 2950, 1780, 1750, 1639, 1245, 1138, 895, 737. The $^1$H- and $^{13}$C-NMR data in Tables I and II. EI-MS $m/z$ (rel. int.): 432 (0.05, $M^+$), 414 (0.2), 319 (21.0), 301 (11.2), 175 (10.3), 123 (43.5), 111 (8.9), 83 (100), 55 (76.5).

**Compound 3 (Ajugacumbin C)** An amorphous powder, $[\alpha]_D^{28}$ +57.7° ($c=0.78$, $CHCl_3$), MW 500 (FAB-MS; 591 $[M+1]$) for $C_{31}H_{42}O_{11}$. UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 215 (4.18). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 2935, 1780, 1738, 1704, 1640, 1369, 1247, 731. The $^1$H- and $^{13}$C-NMR data in Tables I and II. EI-MS $m/z$ (rel. int.): 589 (0.03, $M^+-1$), 558 (0.05), 515 (0.1), 473 (12.1), 310 (23.4), 200 (43.6), 83 (100), 55 (83.7).

**Compound 4 (Ajugacumbin D)** Colorless crystals, mp 183—184 °C (EtOAc–cyclohexane), $[\alpha]_D^{28}$ +33.9° ($c=1.2$, $CHCl_3$), MW 490 (FAB-MS; 491 $[M+1]$) for $C_{27}H_{38}O_8$. UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 218 (4.24). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3450, 2937, 1778, 1732, 1635, 1275, 1252, 1137, 737. The $^1$H- and $^{13}$C-NMR data in Tables I and II. EI-MS $m/z$ (rel. int.): $M^+$ (absent), 441 (2.3), 372 (10.6), 330 (42.4), 313 (29.8), 200 (24.7), 173 (37.1), 83 (100), 55 (74.7).

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