Communications to the Editor

Chem. Pharm. Bull.
31(6)2179—2182(1983)

STRUCTURES OF SHINJULACTONES D AND E, NEW BITTER PRINCIPLES OF *AILANTHUS ALTISSIMA* SWINGLE

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Two bitter quassinoids, shinjulactones D and E (1 and 2), were isolated from *Ailanthus altissima* SWINGLE and their structures were determined to be 11β,20-epoxy-1β,2α,11α,12α-tetrahydroxypicrasan-16-one and 11β,20-epoxy-1β,6α,11α,12α-tetrahydroxypicrasa-3,13(21)-diene-2,16-dione, respectively.

KEYWORDS——quassinoid; shinjulactone D; shinjulactone E; bitter principle; Simaroubaceae; *Ailanthus altissima*; ^{1}H-NMR; ^{13}C-NMR

The structure determination of four bitter principles isolated from *Ailanthus altissima* SWINGLE (Simaroubaceae; Japanese name: Shinju or Niwaurushi) has been reported.[1-4] Two new bitter principles, named shinjulactones D and E (1 and 2), have now been isolated from the same plant. This paper describes the structure determination of 1 and 2.

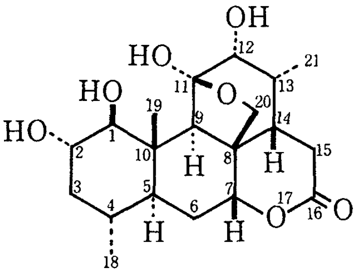
Aqueous extract of root bark of *A. altissima*[5] was continuously extracted with dichloromethane. The organic layer was subjected to separation by silica gel-column chromatography. Gradient elution with chloroform-methanol afforded shinjulactone D (1) in *ca.* 0.001% yield together with other quassinoids.[1,3] Further purification by silicic acid-chromatography followed by crystallization from acetone gave shinjulactone D (1),[6] mp 267-269°C, $[\alpha]_D^{22}$ -44° (c 0.17, pyridine). The molecular formula, $C_{20}H_{30}O_7$, was determined by high resolution mass spectrum. The IR and NMR spectra showed the presence of hydroxyl(s), a δ-lactone, a *t*-methyl, two *s*-methyls, and a hemiacetal group. The UV spectrum gave no characteristic absorption maximum, indicating the absence of any ketone grouping.

Acetylation of shinjulactone D (1) for 20 h at room temperature gave a triacetate (3),[7] mp 135-138°C (sintered at 118-121°C) and prolonged acetylation (for 50 h) a tetraacetate (4),[8] mp 129-132°C.

Investigation on ^{1}H- and ^{13}C-NMR spectra of 1, 3, and 4 together with proton nuclear magnetic double resonance measurement for 1 led to the structure 1 for shinjulactone D. Shinjulactone D (1) showed a doublet signal due to H-1 at δ 3.59 coupled with H-2 with a coupling constant, *J*=9 Hz. The configurations of the vicinal hydroxyl groups were deduced to be 1β-equatorial and 2α-equatorial. The doublet signals due to 12-H were observed at δ 3.76 (*J*=2.5 Hz) and δ 5.03 (*J*=*ca.* 2 Hz) for 3 and 4, respectively, and these coupling constants were almost the same as that (J=3 Hz) reported for chaparrinone triacetate (6)9) derived from chaparrinone (5), this fact indicating that shinjulactone D (1) possesses 12β(equatorial)-H and 13β(axial)-H configurations identical with those for chaparrinone (5). Thus the structure of shinjulactone D (1) was established to be 11β,20-epoxy-1β,2α,11α,12α-tetrahydroxypicrasan-16-one.10)

Shinjulactone E (2) was isolated from bark of *A. altissima*.11) Methanol extract of the bark was partitioned between carbon tetrachloride and water, and the aqueous layer was continuously extracted with dichloromethane. The organic layer was separated by silica gel-chromatography followed by crystallization from methanol-chloroform to afford shinjulactone E (2), amorphous solid, in *ca.* 0.0001% yield. The molecular formula, $C_{20}H_{24}O_8$, of shinjulactone E (2)12) was given by high resolution mass spectrum, which showed the presence of one extra oxygen atom in comparison with ailanthone (7). The ^{1}H-and ^{13}C-NMR spectra revealed the presence of a vinyl methyl, a t-methyl, an *exo*-methylene, an α,β-unsaturated carbonyl, and a lactone grouping. The ^{1}H-NMR spectral data resemble those of ailanthone (7)13) except for a doublet signal at δ 4.87 due to H-7 and a double-doublet signal due to H-6 resonating in a lower field as compared with a signal due to H-6 of ailanthone (7). These observations suggest that the structure of shinjulactone E (2) is 6-hydroxy-substituted ailanthone.

The configuration of the hydroxyl group was determined as follows. Shinjulactone E (2; 22.6 mg) was treated with acetic anhydride and pyridine in the presence of a catalytic amount of *N,N*-dimethylaminopyridine at room temperature for 2.5 d to afford a tetraacetate (8; 6.2 mg),14) mp 112-116°C (from chloroform). The ^{1}H-NMR spectrum showed the presence of a t-methyl, two vinyl methyls, and four



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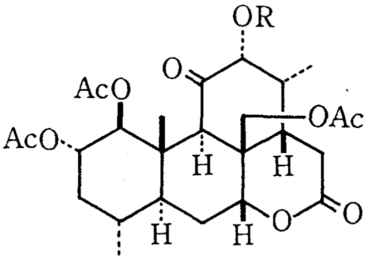
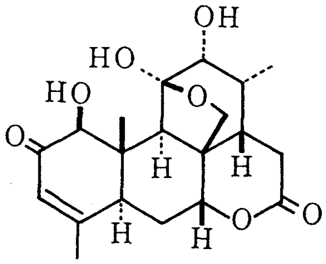


3: R=H
4: R=Ac



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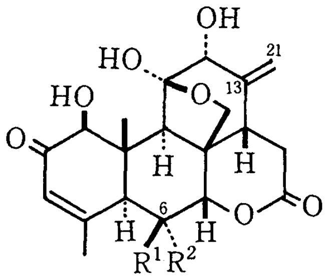
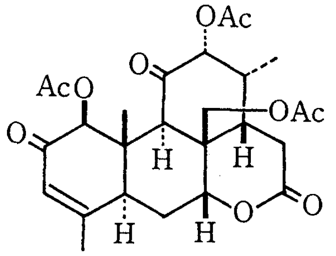


2: R1= H, R2=OH
7: R1=R2=H



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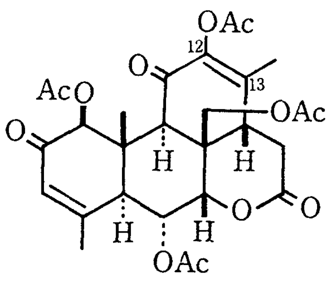

8

acetyl groups and the absence of the *exo*-methylene group. The disappearance of the *exo*-methylene in the acetylation reaction is explained by isomerization of the double bond from $C_{(13)}$-$C_{(21)}$ into $C_{(12)}$-$C_{(13)}$ to afford an enol acetate. This fact is substantiated by seven methyl signals in the ^{13}C-NMR spectrum of 8.

On irradiation at δ 4.84 due to H-7, a double-doublet signal at δ 5.25 due to H-6 of 8 collapsed into a doublet, coupled with an α(axial)-proton on C-5 with a coupling constant, *J*=11.5 Hz. Since the large coupling constant suggests a *trans*-relationship between H-6 and H-5, the H-6 could be determined to be β(axial)-configuration. Thus the structure of shinjulactone E (2) is concluded to be 11β,20-epoxy-1β,6α,11α,12α-tetrahydroxypicrasa-3,13(21)-diene-2,16-dione (= 6-hydroxyailanthone) and its acetate (8) is formulated as 1β,6α,12,20-tetraacetoxypicrasa-3,12-diene-2,11,16-trione.

It is noteworthy that shinjulactones D and E (1 and 2) are the first examples of a perhydroailanthone derivative and $C_{(6)}$-substituted ailanthone, respectively.

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2) T. Furuno, H. Naora, T. Murae, H. Hirota, T. Tsuyuki, T. Takahashi, A. Itai, Y. Iitaka, and K. Matsushita, Chem. Lett., 1981, 1797.
3) M. Ishibashi, T. Murae, H. Hirota, T. Tsuyuki, T. Takahashi, A. Itai, and Y. Iitaka, Tetrahedron Lett., 23, 1205 (1982).
4) H. Naora, T. Furuno, M. Ishibashi, T. Tsuyuki, T. Takahashi, A. Itai, Y. Iitaka, and J. Polonsky, Chem. Lett., 1982, 661.
5) The plant *A. altissima* was collected at the Botanical Gardens, Faculty of Science, the University of Tokyo.
6) IR (KBr):3400, 1730, 1215, and 1050 cm^{-1}; ^{1}H-NMR (C_5D_5N, 270 MHz) δ: 0.83 (3H, d, *J*=6.5 Hz; *s*-CH_3), 1.08 (3H, d, *J*=7 Hz; *s*-CH_3), 1.65 (3H, s; 10-CH_3), 2.95 (1H, s; 9-H), 3.59 (1H, d, *J*=9 Hz; 1-H), 3.73 and 4.14 (each 1H, d, *J*=8 Hz; 20-H), 3.97 (1H, br s; 12-H), *ca.* 4.05 (1H, br m; 2-H), and 4.43 (1H, br s; 7-H); ^{13}C-NMR (C_5D_5N, 67.80 MHz) δ: 11.6q, 13.3q, 20,1q, 26.8t, 29.1d, 30.6t, 31.7d, 41.6s, 42.7s, 42.9d, 43.3t, 44.2d, 46.5d, 70.1d, 71.8t, 79.2d, 79.7d, 85.3d, 110.9s, and 169.9s; MS (EI) m/e (%): 382 (M$^+$; 8), 364 (3), 268 (100), and 250 (60); Found: m/e 382.1969. Calcd for $C_{20}H_{30}O_7$: M 382.1990.
7) IR (KBr): 3530, 2940, 1745, 1725 (sh), 1375, 1240, 1040 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.91 (3H, d, *J*=6.5 Hz; 4-CH_3), 1.13 (3H, d, *J*=7 Hz; 13-CH_3), *ca.* 1.25 (1H, m; 3α-H), 1.36 (1H, ddd, *J*=13, 11, and 2.5 Hz; 5-H), 1.46 (3H, s; 10-CH_3), 1.63 (1H, m; 4-H), 1.76 (1H, ddd, *J*=15, 13, and 2.5 Hz; 6β-H), 1.94, 1.98, and 2.07 (each 3H, s; -$COCH_3$), *ca.* 2.0 (1H, ddd, *J*=15, 2.5, and 2.5 Hz; 6α-H), *ca.* 2.1 (1H, m; 3β-H), *ca.*2.15 (1H, m, 13-H), 2.38 (1H, ddd, *J*=13, 6.5, and 6 Hz; 14-H), 2.74 (1H, dd, *J*=19 and 6.5 Hz; 15β-H), 3.41 (1H, s; 9-H), 3.76 (1H, d, *J*=2.5 Hz; 12-H), 3.85 (1H, dd, *J*=19 and 13 Hz; 15α-H), 3.84 and 4.49 (each 1H, d, *J*=12.5 Hz; 20-H), 4.46 (1H, t, *J*=2.5 Hz; 7-H), 4.70 (1H, d, *J*=9.5 Hz; 1-H), and 5.04 (1H, ddd, *J*=11, 9.5, and 5 Hz; 2-H); ^{13}C-NMR ($CDCl_3$, 22.5 MHz) δ: 12.3, 13.5, 19.1, 20.7, 20.9, 21.5, 25.8, 27.2, 28.3, 35.4, 35.9, 39.0, 41.7, 43.0, 44.8, 48.2, 61.8, 70.8, 77.8, 82.3, 82.6, 170.2, 170.2, 170.4, 174.2, and 212.1; MS (EI) m/e (%): 508 (M$^+$; 13), 488 (25), 466 (8), 406 (25), 376 (42),

316 (50), and 55 (100); Found: m/e 508.2341. Calcd for $C_{26}H_{36}O_{10}$: M 508.2309.

8) IR (KBr): 1745, 1720 (sh), 1370, 1240, and 1040 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 90 MHz) δ: 0.91 (3H, d, *J*= 6.5 Hz; 4-CH_3), 0.97 (3H, d, *J*=6.5 Hz; 13-CH_3), 1.44 (3H, s; 10-CH_3), 1.82, 1.96, 2.08, 2.20 (each 3H, s; -$COCH_3$), 3.17 (1H, s; 9-H), 3.86 and 4.51 (each 1H, d, *J*=13 Hz; 20-H), 4.44 (1H, t, *J*=2.5 Hz; 7-H), 4.70 (1H, d, *J*= 9.5 Hz; 1-H), *ca.* 5.0 (1H, m; 2-H), and 5.03 (1H, d, *J*=*ca.* 2 Hz; 12-H); ^{13}C-NMR ($CDCl_3$, 22.5 MHz) δ: 12.3, 13.0, 19.2, 20.7, 20.7, 20.9, 21.1, 25.6, 27.5, 27.8, 34.2, 35.9, 38.9, 41.7, 43.0, 44.3, 49.5, 61.8, 70.9, 78.1, 80.5, 80.6, 169.5, 169.6, 170.0, 170.2, 171.3, and 204.3; MS (EI) m/e (%): 550 (M^+; 6), 508 (20), 490 (18), 466 (25), 448 (100), 388 (65), and 328 (80); Found: m/e 550.2410. Calcd for $C_{28}H_{38}O_{11}$: M 550.2412.

9) J. Polonsky and N. Bourguignon-Zylber, Bull. Soc. Chim. Fr., 1965, 2793.

10) Numbering of picrasane refers to the nomenclature described in the Chemical Abstracts.

11) The plant, *A. altissima* was collected in Nishinomiya, Hyogo Prefecture.

12) ^{1}H-NMR (C_5D_5N, 90 MHz) δ: 1.70 (3H, s; 10-CH_3), 2.52 (3H, br s; 4-CH_3), 3.64 and 4.27 (each 1H, d, *J*=8 Hz; 20-H), 4.54 (1H, s; 1-H), 4.62 (1H, dd, *J*= 11.5 and 3 Hz; 6-H), 4.87 (1H, d, *J*=3 Hz; 7-H), 5.13 and 5.19 (each 1H, br s; 21-H), and 6.18 (1H, m; 3-H); ^{13}C-NMR (C_5D_5N, 22.5 MHz) δ: 11.5, 26.8, 35.2, 43.7, 46.7, 48.2, 48.2, 48.5, 65.9, 71.7, 80.8, 82.0, 84.5, 110.6, 117.8, 128.1, 147.3, 165.3, 169.3, and 197.2; MS (EI) m/e (%): 392 (M^+; 10), 374 (50), 364 (45), 356 (20), and 314 (100); Found: m/e 392.1462. Calcd for $C_{20}H_{24}O_8$: M 392.1469.

13) ^{1}H-NMR (C_5D_5N + 2% $CDCl_3$, 400MHz) δ: 1.52 (3H, s; 10-CH_3), 1.78 (3H, br s; 4-CH_3), 2.05 (1H br dd, *J*=14 and 13 Hz; 6β-H), 2.22 (1H, br d, *J*=14 Hz; 6α-H), 2.83 (1H, dd, *J*=13 and 5 Hz; 14-H), 2.90 (1H, dd, *J*=18 and 5 Hz; 15β-H), 3.07 (1H, br d, *J*=13 Hz; 5-H), 3.53 (1H, s; 9-H), 3.66 and 4.11 (each 1H, d, *J*=8 Hz; 20-H), 3.69 (1H, dd, *J*=18 and 13 Hz; 15α-H), 4.46 (1H, s; 12-H), 4.54 (1H, s; 1-H), 4.64 (1H, br s; 7-H), 5.19 and 5.28 (each 1H, br s; 21-H), and 6.13 (1H, br s; 3-H). The spectrum of ailanthone (7) was measured by Professor J. Polonsky, CNRS, France, to whom the authors are grateful for the measurement.

14) IR (KBr): 1745, 1680, 1620, and 1235 cm^{-1}; UV $\lambda_{max}^{ethanol}$ 243 nm (ε 12000); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 1.43 (3H, s; 10-CH_3), 1.82 (3H, s; 13-CH_3), 2.03 (3H, br s; 4-CH_3), 2.07, 2.14, 2.17, and 2.22 (each 3H, s; -$COCH_3$), 3.53 (1H, d, *J*=11.5 Hz; 5-H), 4.20 and 4.69 (each 1H, d, *J*=11.5 Hz; 20-H), 4.84 (1H, d, *J*= 3 Hz; 7-H), 5.25 (1H, dd, *J*=11.5 and 3 Hz; 6-H), 5.28 (1H, s; 1-H), and 6.10 (1H, m; 3-H); ^{13}C-NMR ($CDCl_3$, 50 MHz) δ: 13.5q, 15.5q, 20.0q, 20.6q, 20.7q, 21.3q, 24.0q, 29.7t, 39.1d, 42.6s, 44.6d, 46.9s, 48.5d, 61.1t, 66.7d, 77.4d, 83.8d, 127.7s, 129.1d, 159.5s, 167.0s, 169.9s, 170.1s, 171.3s, 174.5s, 179.2s, 190.9s, and 191.7s; MS (EI) m/e (%): 560 (M^+; 10), 518 (65), 476 (80), 458 (50), 416 (85), 315 (90), 297 (80), and 43 (100); Found: m/e 560.1909. Calcd for $C_{28}H_{32}O_{12}$: M 560.1894.

(Received May 31, 1983)