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STRUCTURES OF YADANZIOLIDES A, B, AND C, NEW BITTER PRINCIPLES FROM *BRUCEA JAVANICA*

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Three bitter quassinoids, yadanziolides A, B, and C (1, 2 and 3), were isolated from seeds of *Brucea javanica*, known as "Ya-dan-zi" in Chinese folklore and their structures have been established from chemical transformation and spectral analysis.

KEYWORDS——quassinoid; bitter principle; Simaroubaceae; *Brucea javanica*; ^{1}H-NMR; ^{13}C-NMR

Bitter principles of Simaroubaceous plants have been extensively investigated and a number of quassinoids have been reported.[1] In connection with our studies on bitter principles of *Picrasma ailanthoides* PLANCHON and *Ailanthus altissima* SWINGLE,[2] constituents of seeds of *Brucea javanica* (L.) MERR[3-5] ("Ya-dan-zi" as Chinese drugs) were examined and three new quassinoids, yadanziolides A, B, and C (1, 2 and 3), were isolated together with several known quassinoids.[3-5] This paper describes the structure elucidation of 1, 2, and 3.

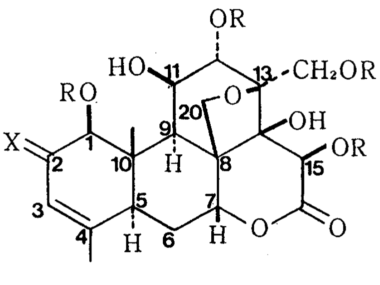
The methanolic extract of defatted seeds of *B. javanica* was partitioned between dichloromethane and water. The aqueous layer was separated by silica-gel chromatography eluted with a lower layer of chloroform-methanol-water (50:12:3). Each fraction was further purified by gel chromatography using Toyopearl HW-40S eluted with methanol and then a Lobar column Lichroprep RP-8 eluted with methanol-water (3:7). These isolation procedures afforded three new quassinoids, yadanziolides A, B, and C (1, 2 and 3).

Yadanziolide A (1; *ca.* 0.01% yield),[6] mp 283-285°C (dec.), $[\alpha]_D^{28}$ -10.5° (*c* 1.7, pyridine) was shown by elemental analysis to have the molecular formula $C_{20}H_{26}O_{10}$. The IR and UV spectra showed the presence of hydroxyl(s), a δ-lactone, and an α,β-unsaturated carbonyl group. Acetylation (acetic anhydride-pyridine) of 1 afforded a tetraacetate (4), $C_{28}H_{34}O_{14}$, mp 202-203°C. Since yadanziolide A (1) was inferred from ^{1}H- and ^{13}C-NMR spectra to be a conjugated ketone corresponding to an oxidation product of brucein F (5),[3] brucein F (5) was treated with MnO_2 in DMF to give the oxidation product, which was identical with 1 in respect to mp, IR, ^{1}H-NMR, and TLC. Thus the structure of yadanziolide A (1) was determined to be 13β,20-epoxy-1β,11β,12α,14,15β,21-hexahydroxypicras-3-ene-2,16-dione.

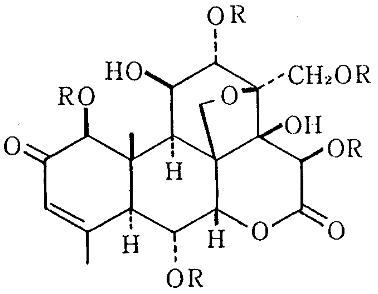
Yadanziolide B (2; *ca.* 0.002% yield),7) mp 279-282°C (dec.), $[\alpha]_D^{23}$ +83° (*c* 4.3, methanol) was shown by elemental analysis to have the molecular formula $C_{20}H_{26}O_{11}$, which possesses one more oxygen atom than 1. The IR and NMR spectra showed the presence of hydroxyl(s), a δ-lactone, an α,β-unsaturated carbonyl, a tertiary methyl, a vinyl methyl, and a hydroxymethyl group. The ^{1}H-NMR spectral data resemble those of yadanziolide A (1) except for a doublet signal at δ 5.67 due to H-7 and a double-doublet signal at δ 4.20 due to H-6 resonating in a lower field compared with a signal due to H-6 of yadanziolide A (1). These observations suggest that the structure of yadanziolide B (2) is 6-hydroxy-substituted yadanziolide A. On irradiation at δ 5.67 due to H-7, the double-doublet signal at δ 4.20 due to H-6 of 2 collapsed into a doublet, coupled with an α(axial)-proton on C-5 with a coupling constant, *J*=11 Hz. Since the large coupling constant suggests a *trans*-relationship between H-6 and H-5, the hydroxyl group was determined to be in 6α (equatrial)-configuration.

Yadanziolide B (2) was acetylated (acetic anhydride-pyridine) to afford a pentaacetate (6), $C_{30}H_{36}O_{16}$, mp 278-283°C (dec.). The ^{1}H-NMR spectrum showed two methyl signals at δ 1.52 (s, 10-CH_3) and 2.03 (br s, 4-CH_3) together with signals due to acetoxyl groups at δ 1.96 (3H, s), 2.09 (6H, s), and 2.22 (6H, s). Thus the structure of yadanziolide B (2) was concluded to be 13β,20-epoxy-1β,6α,11β,12α,14,15β,21-heptahydroxypicras-3-ene-2,16-dione.

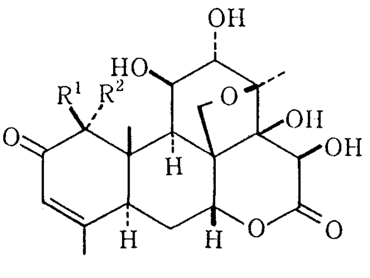
Yadanziolide C (3; *ca.* 0.001% yield),8) mp 292-297°C (dec.), $[\alpha]_D^{23}$ +29° (*c* 1.2, methanol) was shown by elemental analysis to have the molecular formula $C_{20}H_{26}O_9$, which is the same as that of brucein D (7).4,5) The IR and UV spectra showed the presence of hydroxyl(s), a δ-lactone, and an α,β-unsaturated carbonyl group. The ^{1}H-NMR spectrum revealed that the signals of H-5 and H-9 of yadanziolide C (3) shifted to a lower field than those of brucein D (7; see Table I). Comparison of ^{13}C-NMR spectra showed that the signals of C-5 and C-9 of 3 (δ 37.7 and 38.3, respectively) shifted to a higher field than those of 7 (δ 43.6 and 45.8, respectively).



1: R = H, X = O
4: R = Ac, X = O
5: R = H, X = α-OH, β-H



2: R = H
6: R = Ac



3: R^1 = H, R^2 = OH
7: R^1 = OH, R^2 = H

This evidence suggests that the configuration of C-1, C-5, or C-9 might be different from that of brucein D (7). The extensive double resonance experiments at 400 MHz allowed an unambiguous assignment of all protons (Table I). Two broad doublet signals due to H-1 and H-12 were assigned as follows. The two signals at δ 4.46 and δ 4.66 were changed into broad singlets on addition of D_2O. Irradiation at δ 1.63 due to $C_{(10)}$-CH_3 resulted in a slight sharpening of the broad doublet at δ 4.66, while the signal at δ 4.46 remained unchanged. Therefore, the broad doublet signals at δ 4.66 and δ 4.46 are assigned to H-1 and H-12, respectively.

The coupling constants, $J_{5,6\alpha}$=3 Hz and $J_{5,6\beta}$=13.5 Hz, being the same as those of other picrasane derivatives, the proton at C-5 was determined to be in α(axial)-configuration.

The configurations at $C_{(1)}$-H and $C_{(9)}$-H were determined by differential NOE measurement. On saturation of the signal due to $C_{(10)}$-CH_3, increases in area of signals due to $C_{(1)}$-H and one of $C_{(20)}$-H_2 were observed, while an increase in area of the signal due to $C_{(9)}$-H was not detected, indicating $C_{(1\beta)}$-H and $C_{(9\alpha)}$-H orientations.

Thus the structure of yadanziolide C (3) was established to be 13β,20-epoxy-1α,11β,12α,14,15β-pentahydroxypicras-3-ene-2,16-dione, which corresponds to 1-epibrucein D.

It is noteworthy that yadanziolide B (2) possesses as much as eleven *O*-functionalities on the picrasane skeleton, which constitutes the most oxygenated quassinoid, and yadanziolide C (3) is the second example in nature with a 1α-hydroxypicrasane skeleton.9)

Table I. ^{1}H-NMR Spectra of Yadanziolide C (3) and Brucein D (7) in C_5D_5N

	3a)		7b)	
	δ	*J*/Hz	δ	*J*/Hz
1-H	4.66 d	3	4.52 s	
3-H	6.09 br s		6.10 br s	
5-H	3.60 br d	13.5	3.05 br d	13
6α-H	2.38 ddd	13.5, 3, 3	2.30 dt	14, 2
6β-H	1.72 ddd	13.5, 13.5, 3	c)	
7-H	5.52 t	3	5.47 t	2
9-H	3.62 d	5.5	2.84 d	5
11-H	4.97 t	5.5	5.37 d	5
12-H	4.46 d	3	4.30 s	
15-H	6.03 s		6.04 s	
20-H	4.39 d	7.5	4.20 d	8
20-H'	5.01 d	7.5	4.91 d	8
4-CH_3	1.71 br s		1.74 br s	
10-CH_3	1.63 s		1.46 s	
13-CH_3	2.05 s		2.07 s	
-OH	5.50 d	5.5		
	7.05 s			
	7.53 d	3		
	7.66 br s			
	8.23 d	3		

a) Measured at 400 MHz. b) Measured at 90 MHz. c) Not assignable.

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6) IR (KBr): 3430, 1700, 1645, 1620, and 1025 cm^{-1}; UV (methanol) 240 nm (ε 9300); ^{1}H-NMR (C_5D_5N, 90 MHz) δ: 1.43 (3H, s, 10-CH_3), 1.75 (3H, br s, 4-CH_3), 2.31 (1H, dt, J=14, 3 Hz, 6α-H), 2.89 (1H, d, J=5 Hz, 9-H), 3.06 (1H, br d, J=12 Hz, 5-H), 4.29, 5.00 (each 1H, d, J=8 Hz, 20-H), 4.32 (1H, s, 12-H), 4.63, 5.03 (each 1H, d, J=12 Hz, 21-H), 4.71 (1H, s, 1-H), 5.33 (1H, d, J=5 Hz, 11-H), 5.44 (1H, br s, 7-H), 6.06 (1H, s, 15-H), and 6.10 (1H, br s, 3-H); ^{13}C-NMR(C_5D_5N, 22.5 MHz) δ: 11.5q, 22.2q, 28.0t, 43.6d, 45.7d, 48.6s, 50.7s, 64.7t, 70.6t, 70.7d, 75.4d, 78.3d, 79.1d, 83.0d, 83.8s, 84.6s, 124.9d, 163.5s, 174.9s, and 198.4s; MS (EI) *m/z* (%): 426 (M^+; 0.4), 408 (2), 390 (34), 372 (16), 151 (100), and 135 (88); *Anal* Found: C 56.04 %, H 6.16 %. Calcd for $C_{20}H_{26}O_{10}$: C 56.33 %, H 6.15 %.

7) IR (KBr): 3500, 3360, 1710, 1645, 1630 (sh), 1255, 1125, and 1070 cm^{-1}; UV (methanol) 244 nm (ε 10000); ^{1}H-NMR (C_5D_5N, 90 MHz) δ: 1.66 (3H, s, 10-CH_3), 2.51 (3H, br s, 4-CH_3), 2.98 (1H, d, J=5 Hz, 9-H), 3.35 (1H, br d, J=11 Hz, 5-H), 4.20 (1H, dd, J=11, 2 Hz, 6-H), 4.32 (1H, s, 12-H), 4.40, 5.04 (each 1H, d, J=8 Hz, 20-H), 4.68, 5.05 (each 1H, d, J=12 Hz, 21-H), 4.78 (1H, s, 1-H), 5.45 (1H, d, J=5 Hz, 11-H), 5.67 (1H, d, J=2 Hz, 7-H), and 6.20 (2H, s, 3-H and 15-H); ^{13}C-NMR (C_5D_5N, 22.5 MHz) δ: 12.5q, 27.1q, 44.6d, 49.2d, 51.1s, 51.2s, 64.6t, 68.2d, 70.0t, 70.9d, 75.5d, 78.6d, 83.3d, 83.8s, 83.8d, 84.3s, 126.9d, 166.4s, 174.7s, and 198.2s; MS (EI) *m/z* (%): 442 (M^+, 0.8), 424 (12), 406 (28), 388 (10), 378 (36), 360 (12), and 111 (100); *Anal* Found: C 54.11%, H 5.77 %. Calcd for $C_{20}H_{26}O_{11}$: C 54.30 %, H 5.92 %.

8) IR (KBr): 3575, 3550, 3500, 3420, 1705, 1675, 1620, 1160, and 1060 cm^{-1}; UV (methanol) 244 nm (ε 11000); ^{1}H-NMR (Table I); ^{13}C-NMR (C_5D_5N, 22.5 MHz) δ: 15.0q, 19.5q, 22.0q, 28.0t, 37.7d, 38.3d, 44.6s, 49.7s, 70.5d, 70.5t, 73.2d, 76.2d, 79.7d, 82.0s, 82.6s, 85.5s, 125.0d, 161.6s, 174.9s, and 198.4s; MS (EI) *m/z* (%): 410 (M^+, 4), 392 (64), 374 (32), 151 (60), and 135 (100); *Anal* Found: C 58.27 %, H 6.36 %. Calcd for $C_{20}H_{26}O_9$: C 58.53 %, H 6.39 %.

9) cf. castelanolide: R. E. Mitchell, W. Stöcklin, M. Stefanović, and T. A. Geissman, *Phytochemistry*, 10, 411 (1971).

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