Studies on the Constituents of Indonesian *Picrasma javanica*. II.[1] Structure of a New Quassinoid Glucoside, Javanicinoside A

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A new quassinoid glucoside, javanicinoside A was isolated from the bark of *Picrasma javanica* (Simaroubaceae), and its structure was established on the basis of spectroscopic data and an X-ray crystal structure analysis.

Keywords javanicinoside A; quassinoid; *Picrasma javanica*; Simaroubaceae; X-ray crystal structure analysis

Quassinoids, bitter principles of Simaroubaceous plants, have been extensively investigated from the structural viewpoint, because of their useful biological activity.[2] In a continuation of our work on the constituents of *Picrasma javanica* BL.,[1] we have recently isolated a novel quassinoid glucoside from the bark of the plant. This paper deals with the structural elucidation on the basis of spectroscopic data and an X-ray crystal structure analysis of javanicinoside A (**1**).

Results and Discussion

The bark of *P. javanica* collected in Indonesia was extracted with methanol. The *n*-butanol soluble fraction from the methanol extract was chromatographed on Diaion HP-20 eluted with methanol, yielding a mixture of quassinoid fractions. Each fractions was further purified by chromatography on silica gel eluted with chloroform–methanol and then by reversed-phase high-performance liquid chromatography (HPLC) on octadecyl silica (ODS) eluted with methanol–water. These isolation procedures afforded a new quassinoid glucoside, named javanicinoside A (**1**).

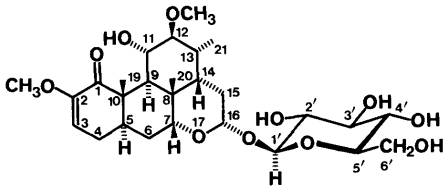

Chart 1

The high-resolution mass spectrum (HRMS) of javanicinoside A (**1**), mp 292 °C, $[\alpha]_D^{27}$ +3.7° (methanol), indicated the formula $C_{27}H_{42}O_{11}$. The infrared (IR) and the ultraviolet (UV) spectra showed the presence of hydroxyl (ν_{max} 3400 cm^{-1}) and α,β-unsaturated carbonyl (ν_{max} 1660 cm^{-1} and λ_{max} 270 nm) absorptions. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed a secondary methyl signal at δ 0.88 (3H, d, J=8 Hz), two tertiary methyl signals at δ 0.94 and 1.34 (each 3H, s) and two methoxyl signals at δ 3.48 and 3.68 (each 3H, s). The ^{1}H–^{1}H two-dimensional (2D) homonuclear and selective proton decoupling NMR experiments revealed the partial structures A, B and the sugar moiety of **1**. The two- and three-bond (C, H) connectivity patterns of **1** were determined by long-range ^{1}H–^{13}C 2D heteronuclear NMR experiments. As shown in Fig. 2, the tertiary methyl protons at δ 1.34 (10-CH_3) were correlated with the ketone at δ 205.86 (C-1) and the methine carbons at δ 37.48 (C-5) and 38.59 (C-9), and the tertiary methyl protons at δ 0.94 (8-CH_3) were correlated with the methine carbons at δ 78.26 (C-7), 38.59 (C-9), and 47.75 (C-14). The anomeric proton at δ 5.33 (H-1′) was correlated with the hemiacetal carbon at δ 99.64 (C-16), and the hemiacetal proton at δ 5.15 (H-16) was correlated with the anomeric carbon at δ 100.56 (C-1′). Some other significant ^{1}H–^{13}C long-range correlations are indicated by arrows in the formula in Fig. 2. An acid hydrolysis of javanicinoside A (**1**) gave two compounds (3 : 2) and D-glucose. The latter was identified as its trimethylsilyl derivative by gas liquid chromatography (GLC). An enzyme hydrolysis of javanicinoside A (**1**) gave one compound and D-glucose.

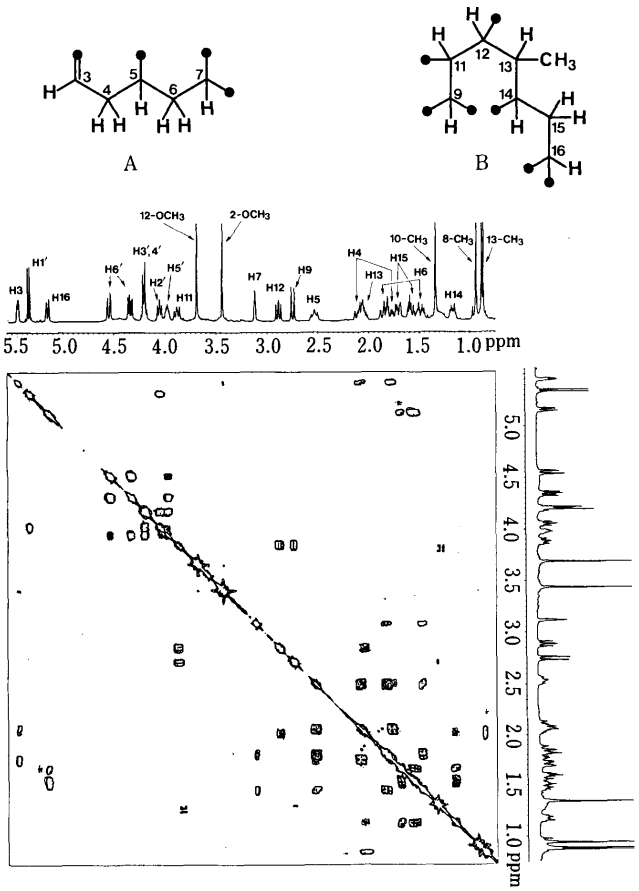

Fig. 1. ^{1}H–^{1}H 2D Homonuclear NMR Spectrum of Javanicinoside A (**1**) and Partial Structures A and B

TABLE I. ^{13}C- and ^{1}H-NMR Spectral Data for Javanicinoside A (**1**)[a,b]

Position	C	H
1	205.86 (s)	
2	149.65 (s)	
3	112.38 (d)	5.45 (1H, dd, J=5, 2 Hz)
4	28.28 (t)	1.79 (1H, ddd, J=20, 5, 4 Hz)
		2.09 (1H, ddd, J=20, 11, 2 Hz)
5	37.48 (d)	2.53 (1H, m)
6	29.71 (t)	1.48 (1H, ddd, J=14, 4, 3 Hz)
		1.85 (1H, ddd, J=14, 10, 2 Hz)
7	78.26 (d)	3.10 (1H, t, J=3 Hz)
8	38.15 (s)	
9	38.59 (d)	2.75 (1H, d, J=11 Hz)
10	48.64 (s)	
11	74.36 (d)	3.88 (1H, dd, J=11, 8 Hz)
12	89.69 (d)	2.86 (1H, t, J=8 Hz)
13	34.95 (d)	2.05 (1H, m)
14	47.75 (d)	1.17 (1H, ddd, J=13, 4, 4 Hz)
15	28.74 (t)	1.56 (1H, ddd, J=14, 13, 9 Hz)
		1.70 (1H, ddd, J=14, 4, 2 Hz)
16	99.64 (d)	5.15 (1H, dd, J=9, 2 Hz)
19 (10-CH_3)	11.30 (q)	1.34 (3H, s)
20 (8-CH_3)	21.50 (q)	0.94 (3H, s)
21 (13-CH_3)	15.22 (q)	0.88 (3H, d, J=8 Hz)
2-OCH_3	54.96 (q)	3.48 (3H, s)
12-OCH_3	60.86 (q)	3.68 (3H, s)
1′	100.56 (d)	5.33 (1H, d, J=8 Hz)
2′	75.02 (d)	4.05 (1H, dd, J=9, 8 Hz)
3′	78.29 (d)	4.20 (1H, m)
4′	71.65 (d)	4.20 (1H, m)
5′	78.64 (d)	3.97 (1H, m)
6′	62.87 (t)	4.43 (1H, dd, J=12, 6 Hz)
		4.55 (1H, dd, J=12, 2 Hz)

a) The spectra were measured in pyridine-d_5. b) s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

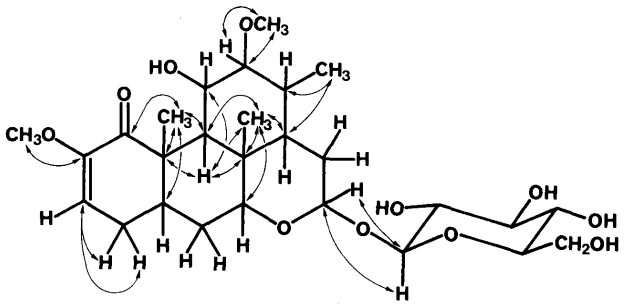

Fig. 2. The Two- and Three-Bond (C, H) Connectivity Pattern Determined by Long-Range ^{1}H–^{13}C Heteronuclear NMR Spectroscopy of Javanicinoside A (**1**)

In order to determine the exact structure of javanicinoside A (**1**), especially the location of the β-D-glucopyranosyl moiety and the absolute stereochemistry, an X-ray crystal structure analysis was undertaken. A crystal of **1** suitable for X-ray analysis was obtained with difficulty from methanol–water. Figure 3 shows a perspective ORTEP drawing of the final X-ray model for the 16-α-*O*-β-D-glucopyranosyl compound **1** showing the absolute stereochemistry of the molecule.

In conclusion, about 150 quassinoids have so far been isolated from Simaroubaceous plants.[2] Although the number and the positions of methyl groups are the same on their basic skeletons and all quassinoids so far known have a methyl group at C-4, javanicinoside A (**1**) lacks the methyl group at C-4. Most of the numerous quassinoids known have the C20 basic skeleton (also named picrasane); this is the first report on the isolation and structure determination of a C-18 norpicrasane quassinoid (javanicinoside A, **1**).

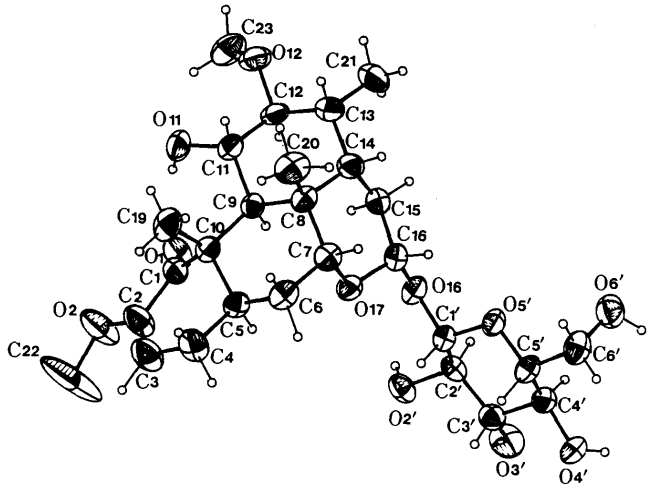

Fig. 3. ORTEP Drawing of Javanicinoside A (**1**) with 50% Probability Ellipsoids

TABLE II. Final Positional Parameters ($\times 10^4$) and Equivalent Isotropic Thermal Parameters with Estimated Standard Deviations in Parentheses for Javanicinoside A (**1**)

Atom	x	y	z	B_{eq} (Å^2)
C(1)	7306 (6)	10450 (2)	5615 (6)	3.3 (1)
C(2)	7826 (7)	819 (3)	6840 (7)	4.7 (1)
C(3)	8988 (7)	942 (3)	7268 (7)	5.1 (2)
C(4)	9836 (6)	1307 (3)	6544 (6)	4.4 (1)
C(5)	9377 (5)	1386 (2)	5158 (6)	3.0 (1)
C(6)	10230 (6)	1761 (2)	4414 (6)	3.4 (1)
C(7)	9805 (6)	1812 (2)	3027 (6)	3.2 (1)
C(8)	8438 (6)	2021 (2)	2920 (6)	2.9 (1)
C(9)	7495 (5)	1673 (2)	3732 (5)	2.5 (1)
C(10)	7927 (5)	1545 (2)	5136 (5)	2.8 (1)
C(11)	6166 (6)	1914 (2)	3609 (6)	3.2 (1)
C(12)	5715 (5)	1886 (2)	2194 (6)	3.2 (1)
C(13)	6629 (6)	2173 (2)	1280 (7)	3.9 (1)
C(14)	8020 (6)	1998 (2)	1476 (6)	3.5 (1)
C(15)	8314 (6)	1463 (3)	873 (6)	3.5 (1)
C(16)	9661 (6)	1307 (2)	1119 (6)	3.3 (1)
C(19)	7642 (7)	1996 (3)	6097 (6)	4.3 (1)
C(20)	8491 (7)	2605 (2)	3316 (8)	4.6 (1)
C(21)	6195 (7)	2116 (3)	−125 (7)	5.5 (2)
C(22)	7480 (1)	141 (4)	8380 (1)	13.4 (3)
C(23)	3437 (7)	1795 (3)	2153 (3)	5.1 (2)
C(1′)	11061 (5)	612 (2)	553 (6)	2.8 (1)
C(2′)	10982 (6)	37 (2)	186 (5)	3.0 (1)
C(3′)	12294 (6)	−173 (2)	−123 (6)	3.2 (1)
C(4′)	12970 (6)	179 (2)	−1079 (6)	3.2 (1)
C(5′)	12960 (6)	747 (2)	−612 (6)	3.3 (1)
C(6′)	13561 (7)	1132 (2)	−1554 (7)	4.0 (1)
O(1)	6464 (4)	807 (2)	5059 (4)	3.8 (9)
O(2)	6989 (5)	473 (2)	7372 (5)	6.9 (1)
O(11)	5224 (4)	1695 (2)	4434 (4)	4.3 (1)
O(12)	4507 (4)	2135 (2)	2053 (4)	4.4 (1)
O(16)	9813 (4)	785 (2)	655 (4)	3.8 (8)
O(17)	9929 (4)	1292 (2)	2473 (4)	3.1 (7)
O(2′)	10464 (4)	−256 (2)	1238 (4)	3.6 (8)
O(3′)	12183 (6)	−692 (2)	−632 (5)	5.1 (1)
O(4′)	14238 (4)	−13 (2)	−1200 (4)	4.3 (1)
O(5′)	11662 (4)	902 (1)	−432 (4)	3.1 (8)
O(6′)	12965 (5)	1128 (2)	−2778 (5)	4.8 (1)

TABLE III. Bond Lengths (Å) with Standard Deviations in Parentheses for Javanicinoside A (**1**)

Atom 1	Atom 2	Distance (Å)	Atom 1	Atom 2	Distance (Å)
C(1)	C(2)	1.50 (1)	C(16)	O(17)	1.218 (7)
C(2)	C(3)	1.34 (2)	C(17)	O(7)	1.450 (7)
C(3)	C(4)	1.49 (2)	C(1)	O(1)	1.218 (7)
C(4)	C(5)	1.530 (9)	C(2)	O(2)	1.363 (9)
C(5)	C(6)	1.521 (8)	O(2)	C(22)	1.44 (1)
C(5)	C(10)	1.578 (8)	C(11)	O(11)	1.422 (7)
C(6)	C(7)	1.512 (9)	C(12)	O(12)	1.427 (7)
C(7)	C(8)	1.537 (8)	O(12)	C(23)	1.424 (8)
C(8)	C(9)	1.575 (8)	C(16)	O(16)	1.423 (8)
C(8)	C(14)	1.563 (9)	C(16)	C(1′)	1.389 (7)
C(8)	C(20)	1.545 (8)	C(1′)	C(2′)	1.517 (8)
C(9)	C(10)	1.561 (8)	C(2′)	C(3′)	1.513 (9)
C(9)	C(11)	1.531 (8)	C(3′)	C(4′)	1.515 (8)
C(10)	C(1)	1.517 (9)	C(4′)	C(5′)	1.528 (9)
C(10)	C(19)	1.551 (9)	C(5′)	C(6′)	1.523 (9)
C(11)	C(12)	1.545 (9)	O(5′)	C(1′)	1.411 (7)
C(12)	C(13)	1.536 (9)	C(2′)	O(2′)	1.430 (7)
C(13)	C(14)	1.54 (1)	C(3′)	O(3′)	1.430 (7)
C(13)	C(21)	1.53 (2)	C(4′)	O(4′)	1.425 (8)
C(14)	C(15)	1.532 (9)	C(5′)	O(5′)	1.434 (7)
C(15)	C(16)	1.494 (9)	C(6′)	O(6′)	1.415 (8)

TABLE IV. Bond Angles (°) with Standard Deviations in Parentheses for Javanicinoside A (**1**)

Atom 1	Atom 2	Atom 3	Angle (°)	Atom 1	Atom 2	Atom 3	Angle (°)
O(1)	C(1)	C(2)	118.4 (6)	C(11)	C(12)	O(12)	110.6 (5)
O(1)	C(1)	C(10)	125.2 (5)	O(12)	C(12)	C(13)	106.3 (5)
C(2)	C(1)	C(10)	116.3 (5)	C(12)	C(13)	C(14)	111.9 (6)
C(1)	C(2)	C(3)	121.7 (6)	C(12)	C(13)	C(21)	110.8 (5)
O(2)	C(2)	C(1)	110.9 (6)	C(14)	C(13)	C(21)	112.3 (6)
O(2)	C(2)	C(3)	127.3 (7)	C(13)	C(14)	C(15)	113.3 (6)
C(2)	C(3)	C(4)	121.7 (6)	C(8)	C(14)	C(13)	112.4 (6)
C(3)	C(4)	C(5)	111.5 (5)	C(8)	C(14)	C(15)	111.7 (5)
C(4)	C(5)	C(6)	112.0 (5)	C(14)	C(15)	C(16)	111.1 (6)
C(4)	C(5)	C(10)	110.6 (5)	C(15)	C(16)	O(17)	111.1 (5)
C(6)	C(5)	C(10)	113.6 (5)	C(15)	C(16)	O(16)	107.3 (5)
C(5)	C(6)	C(7)	111.3 (5)	O(16)	C(16)	O(17)	106.6 (4)
C(6)	C(7)	C(8)	112.1 (5)	C(16)	O(17)	C(7)	110.3 (4)
C(6)	C(7)	O(17)	105.8 (4)	C(2)	O(2)	C(22)	116.3 (6)
C(8)	C(7)	O(17)	111.9 (5)	C(12)	O(12)	C(23)	115.1 (5)
C(7)	C(8)	C(9)	110.8 (4)	C(16)	O(16)	C(1′)	115.4 (4)
C(7)	C(8)	C(14)	108.6 (5)	C(16)	C(1′)	C(2′)	105.9 (4)
C(7)	C(8)	C(20)	106.4 (5)	O(16)	C(1′)	C(5′)	108.1 (4)
C(9)	C(8)	C(14)	108.3 (5)	C(2′)	C(1′)	C(5′)	110.5 (4)
C(9)	C(8)	C(20)	115.2 (6)	C(1′)	C(2′)	C(3′)	110.3 (5)
C(14)	C(8)	C(20)	107.6 (5)	C(1′)	C(2′)	O(2′)	109.5 (4)
C(8)	C(9)	C(10)	115.8 (5)	O(2′)	C(2′)	C(3′)	108.9 (5)
C(8)	C(9)	C(11)	107.7 (4)	C(2′)	C(3′)	C(4′)	110.9 (5)
C(10)	C(9)	C(11)	115.3 (5)	C(2′)	C(3′)	O(3′)	109.4 (6)
C(9)	C(10)	C(1)	110.9 (4)	O(3′)	C(3′)	C(4′)	110.2 (5)
C(9)	C(10)	C(5)	110.3 (4)	C(3′)	C(4′)	C(5′)	110.6 (5)
C(9)	C(10)	C(19)	112.9 (5)	C(3′)	C(4′)	O(4′)	107.1 (5)
C(1)	C(10)	C(5)	101.3 (4)	O(4′)	C(4′)	C(5′)	111.1 (5)
C(1)	C(10)	C(19)	109.3 (5)	C(4′)	C(5′)	C(6′)	113.8 (6)
C(5)	C(10)	C(19)	111.6 (5)	C(4′)	C(5′)	O(5′)	108.1 (5)
C(9)	C(11)	C(12)	109.9 (5)	O(5′)	C(5′)	O(6′)	107.5 (5)
C(9)	C(11)	O(11)	115.4 (5)	C(5′)	C(6′)	O(6′)	112.8 (5)
O(11)	C(11)	C(12)	109.9 (5)	C(2′)	O(5′)	C(5′)	112.1 (4)
C(11)	C(12)	C(13)	111.9 (5)				

Experimental

The melting point was determined on a Yanagimoto micromelting point apparatus and is uncorrected. The UV and IR spectra were recorded with Hitachi 340 and Hitachi 260-30 spectrophotometers, respectively. The ^{1}H- and ^{13}C-NMR spectra were recorded with a JEOL GX-400 (^{1}H-NMR at 400 MHz and ^{13}C-NMR at 100 MHz) spectrometer. Chemical shifts are given on the δ-scale (ppm downfield from tetramethylsilane as an internal standard) and coupling constants in hertz (Hz). MS and HRMS were run on a JEOL JMS-DX-303 mass spectrometer. Optical rotation was determined on a JASCO DIP-4. Thin-layer chromatography was carried out on Silica gel $60F_{254}$ and reversed-phase Rp-8 (Merck). Diaion HP-20 (Mitsubishi Kasei) and silica gel (BW-820MH, Fuji Davison) were used for column chromatography. HPLC was carried out on an ODS column (Capcell pak ODS, Shiseido, 10 m/m i.d. × 250 mm).

Extraction and Isolation Dried bark (1.8 kg) of *Picrasma javanica* collected at Kebun Raya Bogor, Indonesia, in July 1986, was extracted with MeOH (16 l). The extract was concentrated under reduced pressure to give a residue (263 g), to which an equal volume of water was added. The aqueous solution was extracted with $CHCl_3$ (4 l) and then *n*-BuOH (4 l). The *n*-BuOH-soluble fraction (38 g) was applied to a column of Diaion HP-20 (1.5 kg). Elution with MeOH gave fractions 1—20. Fractions 11—18 (10 g) were chromatographed on a silica gel (500 g) column. Elution was performed with 1, 5, 10, 25, and 50% MeOH in $CHCl_3$ and MeOH. The 25% MeOH in $CHCl_3$ fraction (3.8 g) was subjected to preparative HPLC using Capcell pak ODS with a mixed solvent, H_2O–MeOH (3 : 2, v/v), to afford jávanicinoside A (**1**; 35 mg).

Javanicinoside A (1) Colorless prisms (MeOH–H_2O), mp 292 °C, $[\alpha]_D^{27}$ +3.7° (c = 1.1, MeOH). UV λ_{max}^{MeOH} nm (log ε): 270 (3.56). IR ν_{max}^{KBr} cm^{-1}: 3400, 1660, 1638, 1080, 1040. ^{1}H- and ^{13}C-NMR: see Table I. MS *m/z*: 542 (M^+, 20%), 380 (9), 372 (45), 362 (100), 345 (34), 330 (37), 314 (51), 299 (61), 285 (15), 271 (22), 253 (17), 203 (23), 187 (13), 151 (22), 127 (34), 107 (24), 95 (30), 73 (51), 60 (31), 43 (43). HRMS: Found *m/z* 542.2730. Calcd for $C_{27}H_{42}O_{11}$, *m/z* 542.2727.

Acid Hydrolysis of Javanicinoside A (1) A solution of javanicinoside A (**1**; 5 mg) in 1.5 M H_2SO_4 (2 ml) and MeOH (4 ml) was refluxed for 5 h. After cooling of reaction mixture, water (5 ml) was added and the product was extracted with $CHCl_3$ (5 ml × 3 times). The $CHCl_3$ extract showed two peaks (3 : 2) in HPLC using Capcell pak ODS and a solvent mixture of MeOH–H_2O (3 : 2). The water layer was neutralized with anion-exchange resin (Amberlite IRA-402), evaporated, and dried on P_2O_5 to give a residue (sugar) which was identified as α- and β-D-glucose (as the trimethylsilyl (TMS) derivatives) by GLC (SE-30, 2%, 150 °C).

Enzyme Hydrolysis of Javanicinoside A (1) A solution of javanicinoside A (**1**; 3 mg) and β-glucosidase (20 mg, from almond, Sigma) was adjusted to pH 5.0 (dilute HCOOH, 10 ml) and incubated at 37 °C 78 h. After cooling, the reaction mixture was extracted with $CHCl_3$. The organic layer showed one peak in HPLC using the method described above. The water layer was dried and the residue obtained was converted into the TMS derivative of D-glucose (identified by GLC as described above).

X-Ray Crystal Structure Analysis of Javanicinoside A (1) Javanicinoside A (**1**) crystallized in orthorhombic space group $P2_12_12_1$, with the lattice parameters a = 10.513 (6), b = 25.498 (11), and c = 10.375 (2) Å. V = 2781.3 Å^3; Z = 4; D_{calc} = 1.296 g·cm^{-3}; D_{obs} = 1.324 g·cm^{-3}. Intensity data were measured on an Enraf-Nonius CAD-4 diffractometer using monochromated Cu $K\alpha$ radiation. A total of 2804 independent structure factors with $I_0 > 3\sigma(I_0)$ within $4 \leqq 2\theta \leqq 150°$ were obtained in the 2θ–ω scanning mode. The structure was solved by the direct method using the structure determination package SDP. The structure was refined by the full-matrix least-squares method to the final R factor of 0.058. The final parameters are listed in Table II, and bond lengths and bond angles are listed in Tables III and IV, respectively, along with their standard deviations.

References

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