Communications to the Editor

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YANDANZIOLIDE D, A NEW C_{19}-QUASSINOID ISOLATED FROM *BRUCEA JAVANICA* (L.) MERR

Shin Yoshimura,[*,a] Keiichiro Ogawa,[a] Takahiko Tsuyuki,[*,b] Takeyoshi Takahashi,[b] and Tadashi Honda[c]

Department of Chemistry, The College of Arts and Sciences, The University of Tokyo,[a] Komaba, Meguro, Tokyo 153, Japan, Department of Chemistry, Faculty of Science, The University of Tokyo,[b] Hongo, Bunkyo, Tokyo 113, Japan, and Suntory Institute for Biomedical Research,[c] Wakayamadai, Shimamotocho, Mishimagun, Osaka 618, Japan

A new quassinoid, yadanziolide D, was isolated from *Brucea javanica* (L.) MERR and the structure was determined to be (5*S*,10*S*)-13β,20-epoxy-11β,12α,14,15β-tetrahydroxy-16-oxo-1,2-seco-1-nor-6(5→10)*abeo*-picras-3-en-2,5-olide by the combined analysis of its various spectroscopic data and the X-ray analysis of its di-*O*-acetyl derivative using the Patterson fragment search.

KEYWORDS——quassinoid; bitter principle; Simaroubaceae; *Brucea javanica*; ^{1}H-NMR; X-ray analysis

Seeds of *Brucea javanica* (L.) MERR, known as 'Ya-dan-zi' in Chinese folklore, have been used as a Chinese medicine for the treatment of cancer, and the main components with antileukemic activity have been investigated by Geissman,[1] Polonsky,[2] and Lee *et al.*[3] In our continuing studies on the bitter principles of Simaroubaceous plants, we examined the minor components of 'Ya-dan-zi', and reported three new quassinoids,[4] yadanziolides A-C, and sixteen new quassinoid glycosides,[4,5] yadanziosides A-P. Further investigation led to the isolation of a new bitter C-19 quassinoid named yadanziolide D (1), the structure of which is described in this paper.

The methanolic extract of defatted seeds of *B. javanica*[4] was partitioned between dichloromethane and water, and the organic layer was subjected to separation by silica-gel chromatography. Fractions eluted with a lower layer of chloroform-methanol-water (50:12:3) were further separated by silica-gel chromatography, gel chromatography, and reversed phase chromatography to afford yadanziolide D (1; *ca.* 0.001% yield),[6] mp 280-282 °C, $[\alpha]_D^{22}$ -7.5° (*c* 1.0, methanol); Found: *m/z* 396.1405. Calcd for $C_{19}H_{24}O_9$: *M* 396.1420.

On spectral comparison with known quassinoids, yadanziolide D (1) appeared to have a 1,2-seco-1-nor-6(5→10)*abeo*-picrasane skeleton, which has been found only in shinjulactone B (2)[7] isolated from *Ailanthus altissima* SWINGLE (Japanese name: Shinju or Niwaurushi). The existence of a $C_5H_5O_2$ moiety was indicated by the fragment peaks at *m/z* 299 (M- $C_5H_5O_2$)$^+$, 281 (M- $C_5H_5O_2$-H_2O)$^+$, and 97 ($C_5H_5O_2$)$^+$ in the mass spectrum and by its IR, UV and ^{13}C-NMR spectra which show characteristic patterns due to the α,β-unsaturated lactone. All of the signals for 1 in the ^{1}H-NMR spectrum (see Table I) were assigned with its COSY spectrum and the structures of C, D, and E rings were suggested to be the same as those of brucein D (3).[3,8]

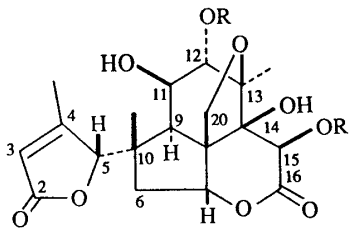
In the NOESY spectrum at 400 MHz, the NOE's were observed from $C_{(10)}$-CH_3 to 20-H, from 9-H to 5-H and 15-H, and from 6α-H to $C_{(4)}$-CH_3. These observations can be interpreted on the assumption that C-5 has an *S*-configuration.

Unambiguous proof for the structure of yadanziolide D (1) was provided by single crystal X-ray analysis of its di-*O*-acetyl derivative (4).

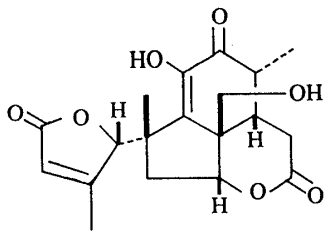
Acetylation of **1** with acetic anhydride in pyridine gave a 12,15-di-*O*-acetyl derivative (**4**),[9] mp 289-294 °C, which crystallized from methanol-diethyl ether. Crystals of **4** belong to an orthorhombic space group $P2_12_12_1$ with the cell parameters of a = 15.365(3), b = 20.566(4), c = 7.107(1) *angstrom*, Z = 4, and D_c = 1.421 g cm^{-3}. The structure could not be solved after many attempts by the direct method using the MULTAN[10] and SHELXS,[11] but was solved by the Patterson fragment search method using PATSEE.[12] This method requires a good input structure and was carried out as follows; the structure (**4**), which was inferred from examination of its solution spectra, was optimized by molecular mechanics calculations using Allinger's MMP2,[13] and a cutoff of the A-ring and two acetyl groups from the optimized structure gave the input structure for PATSEE. After the structural refinement, the R factor was 0.088. Fig. 1 shows a computer-genarated perspective drawing of the molecule **4**, indicating 5*S* and 10*S* configurations. Thus the structure of yadanziolide D (**1**) was established to be (5*S*,10*S*)-13β,20-epoxy-11β,12α,14,15β-tetrahydroxy-16-oxo-1,2-seco-1-nor-6(5→10)*abeo*-picras-3-en-2,5-olide.

The structure determination procedure described above shows one of the typical cases where neither the analysis of solution phase spectra alone nor the X-ray analysis alone is successful, but the combination of the two methods leads to success. In this case, good molecular mechanics calculations play an essential role as well as other experimental methods.

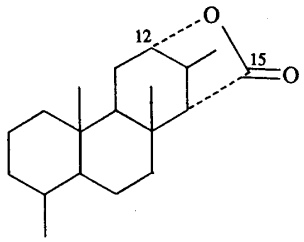
For the C-19 quassinoids, only two basic skeletons have been reported; one is a 16-norpicrasan-15,12α-olide skeleton [A], and the other a 1,2-seco-1-nor-6(5→10)-*abeo*-picrasan-2,5-olide skeleton [B]. While the former has been found in several C-19 quassinoids such as samederin B[14] or eurycomalactone,[15] the latter has been found only in shinjulactone B (**2**).[7] One of the most interesting features in the structure of **1** is that the configration of C-5 is opposite to that of **2**. This fact may suggest that the direction of the α,β-unsaturated γ-lactonization in the hypothetical biogenetic pathway from a precursor (**3**) to **1** is opposite to that from ailantone (**5**) to **2**.[7]



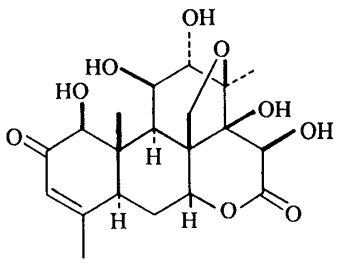
1 R = H
4 R = Ac



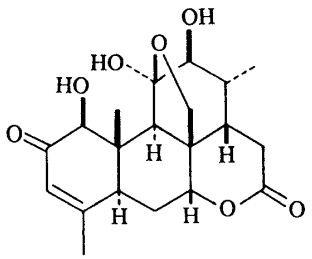
2



A



3



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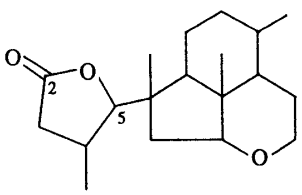

B

Table I. ^{1}H-NMR Spectra of Yadanziolide D (1) and 12,15-di-*O*-Acetylyadanziolide D (4)

	1			4		
	δ		*J*/Hz	δ		*J*/Hz
3-H	5.96	br s		5.93	br s	
5-H	4.96	s		4.84	br s	
6α-H	2.44	d	15.4	2.64	d	15.7
6β-H	1.80	dd	15.4, 5.1	1.87	dd	15.7, 4.9
7-H	5.29	d	5.1	5.03		
9-H	3.35	d	4.0	2.63	d	4.3
11-H	5.15	d	4.0	4.39	d	4.3
12-H	4.53	s		5.03		
15-H	6.32	s		6.35	s	
20-H	4.42	d	6.2	4.06	d	6.6
20-H'	4.88	d	6.2	4.44	d	6.6
4-CH_3	1.92	br s		2.14	br s	
10-CH_3	1.39	s		1.16	br s	
13-CH_3	2.07	s		1.26	s	
12-OAc	-			2.25	s	
15-OAc	-			2.07	s	
	400 MHz	C_5D_5N		270 MHz	$CDCl_3$	

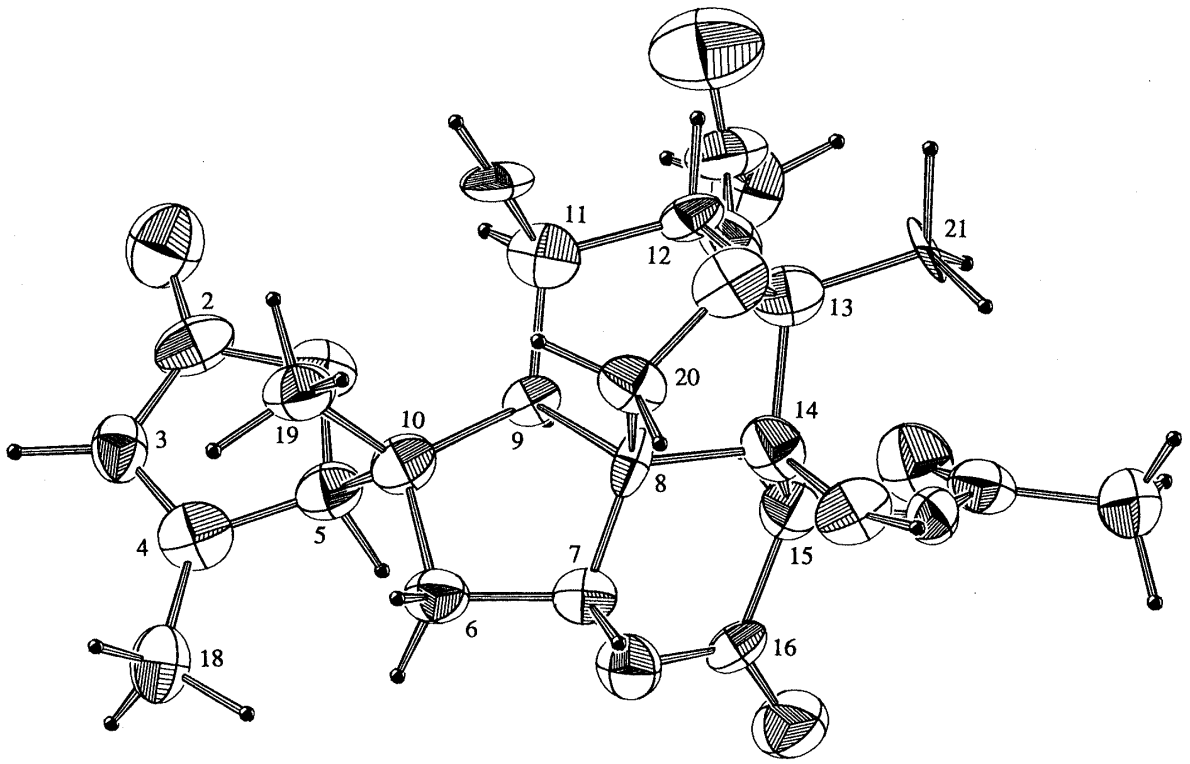

Fig. 1. ORTEP Drawing of 12,15-di-*O*-Acetylyadanziolide D (4)

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6) **1**: IR (KBr) 3450, 1740, 1640, 1385, 1135, 1080, and 1045 cm^{-1}; ^{13}C-NMR (C_5D_5N, 22.5 MHz) δ = 11.5q, 18.6q, 21.3q, 44.7t, 46.9s, 48.5d, 69.1s, 70.3d, 75.6d, 79.7s, 81.1t, 83.7d, 84.1d, 86.7s, 94.0d, 120.0d, 167.8s, 172.5s, and 174.5s; MS (EI) *m/z* (%) 396 (M^+; 2), 378 (6), 360 (5), 321 (8), 303 (5), 299 (5), 281 (36), 263 (26), 125 (100), and 97 (50).

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9) **4**: IR (KBr) 3480, 1760, 1750, 1640, 1380, 1240 and 1040 cm^{-1}; MS (CI, CH_4) *m/z* (%) 481 (MH^+; 100), 421 (75), 403 (30), 379 (18), 361 (32), 99 (25), and 61 (70); HRMS (EI) Found: *m/z* 462.1540. Calcd for $C_{23}H_{26}O_{10}$ (M - H_2O): *m/z* 462.1527.

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