Communications to the Editor

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ISOLATION AND STRUCTURES OF HEDYOTISOL-A, -B, AND -C NOVEL DILIGNANS FROM *HEDYOTIS LAWSONIAE*

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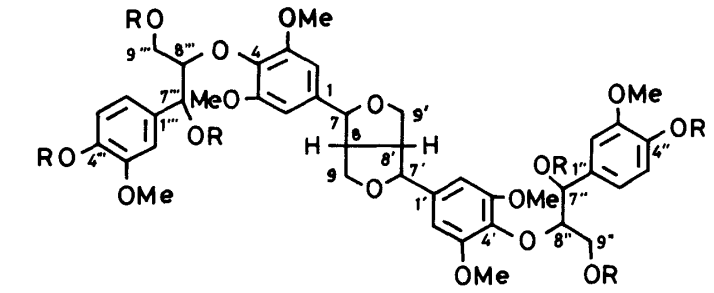
Three new dilignans, hedyotisol-A (1a), -B (2a), and -C (3a), were isolated from the leaves of *Hedyotis lawsoniae* and their structures were examined. These compounds are constructed from a syringaresinol unit and two phenylpropane units, and they are stereoisomeric with each other.

KEYWORDS —— *Hedyotis lawsoniae*; lignan; dilignan; hedyotisol-A; hedyotisol-B; hedyotisol-C

In a previous paper,[1] we reported the isolation and structure determination of new sesquilignans, hedyotol-A, -B, -C, and -D, from *Hedyotis lawsoniae* (DC.) Wight et Arn. (Rubiaceae). This communication describes the structures of three new dilignans, hedyotisol-A (1a), -B (2a), and -C (3a), which are minor components isolated from the leaves of *H. lawsoniae*.

The ethyl acetate-soluble portion of the methanolic extract of dried leaves (0.98 kg) of this plant was roughly fractionated by silica gel column chromatography and the fractions 52-53[1] eluted with MeOH-$CHCl_3$ (1:9) were separated into neutral and acidic portions.[2] The latter was acetylated in the usual way and the acetate mixture was further purified by centrifugal silica gel chromatography and preparative layer chromatography to give hedyotisol-A hexaacetate (1b) (3.7 mg), -B hexaacetate (2b) (2.0 mg), and -C hexaacetate (3b) (1.1 mg), along with (-)-dehydrodiconiferyl alcohol triacetate.[1]

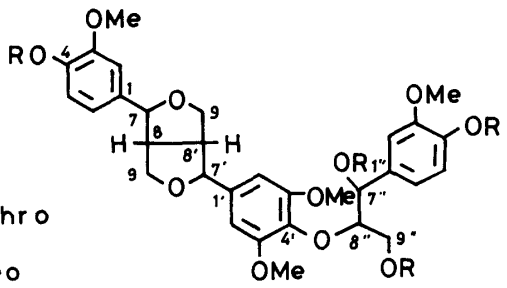
Hedyotisol-A hexaacetate (1b), amorphous powder, has the molecular formula $C_{54}H_{62}O_{22}$, and shows UV absorption maxima at 273.5 and 279 nm (log ε 3.92 and 3.90, respectively) and IR absorptions at 1760, 1740, 1240 (acetoxyl), 1600, and 1510 cm^{-1} (phenyl). The ^{1}H-NMR spectrum of 1b exhibits characteristic signals ascribable to a 3,7-dioxabicyclooctane grouping (I) and a glycerol grouping (II, *erythro* form)[3] together with signals due to acetoxyl, methoxyl, and phenyl protons as shown in Table I. These spectral data are very similar to those of hedyotol-C tetraacetate (4b), but the intensities of the ^{1}H-NMR signals of the benzylic proton in II (δ 6.10, br d) and of the aliphatic acetoxyls (δ 2.00, 2.16) are approximately double those of 4b. Therefore, it was deduced that 1b has two units of structure II. Furthermore, the presence of two symmetrically substituted phenyl groups (IV) in 1b was suggested by the appearance of two singlets due to four aromatic protons and four methoxyl groups (δ 6.52 and 3.76, respectively), and also the presence of two 1,3,4-



1 : 7'',8''- , 7''',8'''- erythro

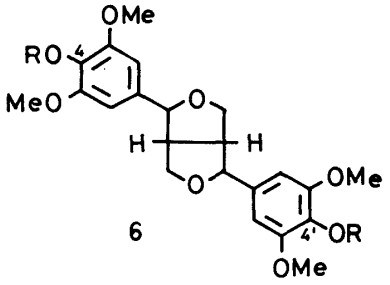
2 : 7'',8''- erythro,
7''',8'''- threo

3 : 7'',8''- , 7''',8'''- threo



4 : 7'',8''- erythro

5 : 7'',8''- threo



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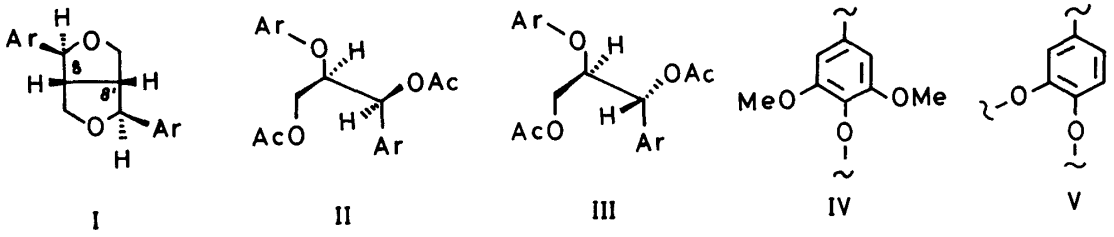
(a : R=H, b : R=Ac)



I II III IV V

Chart 1

trisubstituted phenyl groups (V) was indicated by the signals at δ 6.94-7.01 due to aromatic protons (Table I). Besides, the structure of 1b may be highly symmetric in view of the ^{1}H-NMR spectral pattern.

The MS of 1b failed to give the molecular ion peak, but it gave significant fragment peaks at *m/z* 418 (VI: Found 418.1610, Calcd for $C_{22}H_{26}O_8$, 418.1626), 323 (VII: Found 323.1101, Calcd for $C_{16}H_{19}O_7$ 323.1130), 222 (VIII: Found 222.0897, Calcd for $C_{12}H_{14}O_4$ 222.0902), and 179 (VIII-43: Found 179.0628, Calcd for $C_{10}H_{11}O_3$ 179.0707), along with peaks at *m/z* 181 (IX) and 167 (X) which are characteristic of syringaresinol type lignans (6).[1,4]

From the above spectral data and biogenetic considerations, hedyotisol-A was believed to be a dilignan constructed from syringaresinol (6a) and two 1-(4-hydroxy-3-methoxyphenyl)propane-1,2,3-triol groups.[5] Its structure should be represented by formula 1a.

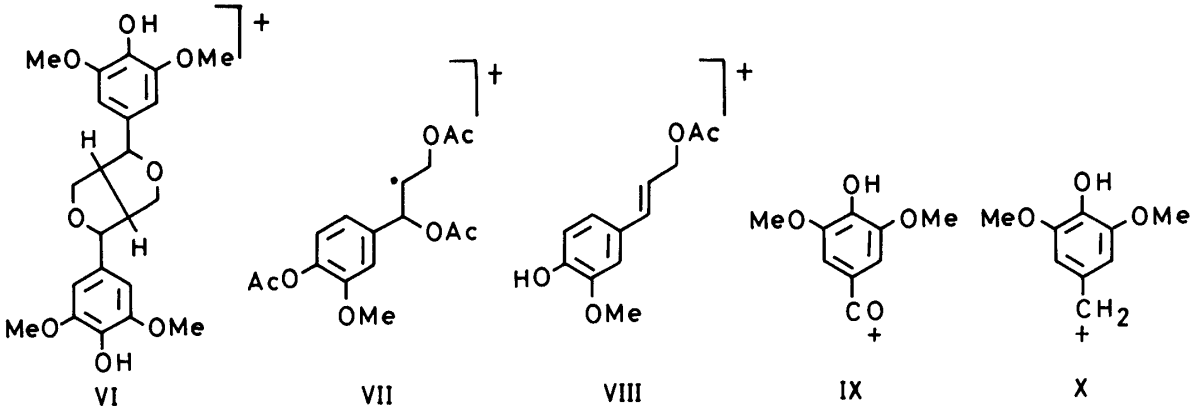
Hedyotisol-B hexaacetate (2b), $C_{54}H_{62}O_{22}$, and -C hexaacetate (3b) were obtained as amorphous powder and both show the UV, IR, and MS spectra almost superimposable

Table I. ^{1}H-NMR (200 MHz) Spectral Data of New Dilignan Hexaacetates and Sesquilignan Tetraacetates from *H. lawsoniae* (δ in $CDCl_3$)

Compound / Proton	1b	2b	3b	4b[1)]	5b[1)]
Dioxabicyclo-octane portion					
7-, 7'-H	4.73 (2H,br d) (4.5 Hz)	4.73 (2H,br d) (4.5 Hz)	4.74 (2H,br d) (4.5 Hz)	4.84 (1H,d) (5.0 Hz)	4.84 (1H,d) (5.0 Hz)
				4.73 (1H,d) (5.0 Hz)	4.75 (1H,d) (5.0 Hz)
8-, 8'-H	3.09 (2H,m)	3.09 (2H,m)	3.08 (2H,m)	3.10 (2H,m)	3.10 (2H,m)
9-, 9'-H_2	3.93 (2H,dd) (9, 3.5 Hz)	3.9-4.0 (2H,m)	3.93 (2H,dd) (9, 3.5 Hz)	3.89-3.98 (2H)	3.91-3.99 (2H)
	4.22-4.40 (2H)[a)]	4.22-4.65 (2H)[a)]	4.25-4.40 (2H)[a)]	4.21-4.37 (2H)[a)]	4.25-4.42 (2H)[a)]
Glycerol portion					
7",7'"-H	6.10 (2H,br d) (5.0 Hz)	6.10 (1H,br d) (5.0 Hz)		6.11 (1H,br d) (5.0 Hz)	
		6.18 (1H,d) (6.2 Hz)	6.17 (2H,d) (6.2 Hz)		6.19 (1H,d) (6.2 Hz)
8"-,8'"-H	4.63 (2H,m)			4.63 (1H,m)	
		4.22-4.65 (6H)[a)]	4.52 (2H,m)		4.55 (1H,dt) (6.2, 4.5 Hz)
9"-,9'"-H_2	4.22-4.40 (2H)[a)]			4.21-4.37 (1H)[a)]	
			4.25-4.40 (4H)[a)]		4.25-4.42 (2H)[a)]
	4.49 (2H,dd) (12, 5.5 Hz)			4.49 (1H,dd) (12, 5.5 Hz)	
Alcoholic acetoxyl	2.00 (6H,s)	2.00 (3H,s)		1.99 (3H,s)	
		2.01 (3H,s)	2.01 (6H,s)		2.01 (3H,s)
		2.02 (3H,s)	2.02 (6H,s)		2.02 (3H,s)
	2.16 (6H,s)	2.16 (3H,s)		2.14 (3H,s)	
Phenolic acetoxyl	2.30 (6H,s)	2.30 (3H,s)		2.29 (3H,s)	
		2.31 (3H,s)	2.31 (6H,s)		2.31 (3H,s)
				2.32 (3H,s)	2.33 (3H,s)
Methoxyl	3.76 (12H,s)	3.76 (6H,s)		3.77 (6H,s)	
		3.78 (6H,s)	3.78 (12H,s)		3.80 (6H,s)
	3.82 (6H,s)	3.82 (3H,s)		3.81 (3H,s)	
		3.83 (3H,s)	3.82 (6H,s)		3.83 (3H,s)
				3.86 (3H,s)	3.87 (3H,s)
Aromatic	6.52 (4H,s)[b)]	6.52 (2H,s)[b)]		6.52 (2H,s)[b)]	
		6.54 (2H,s)[b)]	6.53 (4H,s)[b)]		6.54 (2H,s)[b)]
	6.94 (2H,br d) (8.0 Hz)				
		6.9-7.1 (6H)	7.00 (4H,br s)	6.87-7.06 (6H)	6.90-7.12 (6H)
	6.97 (2H, d) (8.0 Hz)				
	7.01 (2H, br s)		7.09 (2H,br s)		

a) Detailed analysis could not be done because of the signal overlapping in each compound.

b) Slightly broadened by the long range coupling with 7- and/or 7'- proton.



VI VII VIII IX X

Chart 2

on those of 1b. Their ^{1}H-NMR spectra are also similar to that of 1b, but they are slightly different with each other as shown in Table I. Especially, in the ^{1}H-NMR spectrum of 2b, the signals at δ 6.10-6.18 assignable to the benzylic protons in the glycerol grouping and the signals at δ 2.00-3.83 due to the acetoxyl and methoxyl groups appear in fairly complex pattern, whereas the corresponding signals of 3b are rather simple and they resemble those of hedyotol-D tetraacetate (5b) which has the *threo* glycerol grouping (III). This fact suggests that 2b has glycerol groupings II and III, while 3b contains two glycerol groupings III in the molecule.

Based on the above spectral evidence and the biogenetic analogy, hedyotisol-B and -C are stereoisomeric with hedyotisol-A (1a) and their structures should be represented by the formula 2a and 3a, respectively. These three dilignans are optically inactive, though (+)-syringaresinol was isolated from the same source.

It should be noted that two dilignans were previously obtained from *Arctium lappa* L.[6] and this is the second time that dilignans have been isolated from the natural source.

REFERENCES AND NOTES

1) T. Kikuchi, S. Matsuda, S. Kadota, and T. Tai, *Chem. Pharm. Bull.*, in press.
2) Since the crude acidic fraction showed no acetyl signal in the ^{1}H-NMR spectrum, hedyotisol-A, -B, and -C have no acetyl group.
3) The relative configuration of II and III can be assigned on the basis of the ^{1}H-NMR data. See F. Nakatsubo, K. Sato, and T. Higuchi, *Mokuzai Gakkaishi*, 22, 29 (1976) and references cited therein.
4) A. Ichihara, Y. Numata, S. Kanai, and S. Sakamura, *Agric. Biol. Chem.*, 41, 1813 (1977); A. Pelter, *J. Chem. Soc.* C, 1967, 1376.
5) This conclusion is based mainly on the biogenetic analogy with hedyotol-C and -D and the alternative possibility of the 1-(3-hydroxy-4-methoxyphenyl)propane-1,2,3-triol group could not be excluded at present.
6) A. Ichihara, S. Kanai, Y. Nakamura, and S. Sakamura, *Tetrahedron Lett.*, 1978, 3035.

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