5'-METHOXYYATEIN AND 5'-METHOXYPODORHIZOL NEW LIGNANS ISOLATED FROM HERNANDIA CORDIGERA VIELL.[1]

Pascal Richomme and Jean Bruneton* (CEPM, U.E.R. de Pharmacie, 16 Boulevard Daviers, 49000-Angers, France)
Adrien Cavé (CCIPE, BP 5055, 34033-Montpellier Cedex, France)

Abstract - Two new dibenzylbutyrolactone lignans have been isolated from Hernandia cordigera : 5'-methoxyyatein and 5'-methoxypodorhizol. Their structures have been determined by means of high resolution ^1H nmr spectra, CD curves and acidic cyclization.

Leaves and barks of Hernandia cordigera (Hernandiaceae) are rich in lignans.[2] The main compound has been found to be desoxypodophyllotoxin 1. We wish now to report two new dibenzylbutanolides: the 5'-methoxyyatein 2 and the 5'-methoxypodorhizol 5.

The lignans were isolated using the method reported in our precedent publication[1]. 2 and 5 were obtained pure by TLC.

The 5'-methoxyyatein 2, $C_{23}H_{26}O_8$, α_D: -21° ($CHCl_3$, c=1), was obtained as an amorphous powder. Its ir spectrum shows the presence of a lactone (ν 1760 cm^{-1}). The ^1H nmr spectrum indicates a substitution by four aromatic methoxyl groups (δ 3.82, 3.83 (6H) and 3.85 ppm). These data and the fragmentation as obtained in the mass spectrum (m/z 181 and 165) are characteristic of a butenolide substituted in C-2 and C-3 by a trimethoxybenzyl group and a methoxy-methylenedioxybenzyl group.[3] The major ion at m/z 181, resulting from a cleavage of the C-2 - C-6 bond and the ions at m/z 191 and 238 supplied a clear cut answer to the substitution pattern of 2, which is the 2-(3",4",5"-trimethoxybenzyl)-butyrolactone.[4,5] The relative configuration in C-2 and C-3 can be established by a further study of the ^1H nmr spectrum. The coupling constants J_{3-4a} and J_{3-4b} are almost equiva-

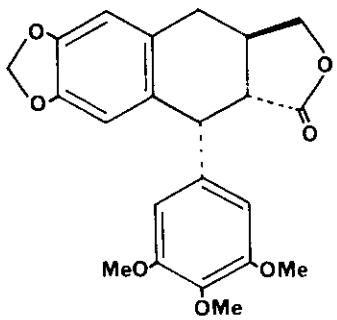
lent (7.0 Hz and 7.2 Hz respectively), which indicates that a trans relationship prevails between the two benzylic groups.[5] The different chemical shifts for H-4a (δ 3.87 ppm) and for H-4b (4.18 ppm) and the equivalence of the protons in C-6 and C-5 confirm the 2-3 trans configuration.[6,7] 2 has the 2R,3R configuration since its CD curve is similar to that of yatein 3 and of bursehenin 4,[8,9,10] whose ^{1}H nmr and ^{13}C nmr spectra are also closely related to this of 2 (Tab. 1).

The second lignan isolated 5 shows spectral data which point to a close relationship with compound 2.[7] The ir spectrum displays, besides the absorption due to the lactone, a band at ν 3435 cm^{-1} characteristic for a hydroxyl group. The ^{1}H nmr spectrum indicates the same substitution pattern on the two benzylic groups as in lignan 2. The mass spectrum shows a molecular ion at m/z 446 ($C_{23}H_{26}O_9$) meaning that 5 contains one oxygen more than 2. The base peak is at m/z 197, corresponding to the ion a instead of 181 as in the mass spectrum of 2; therefore, the hydroxyl group must be in the C-6 position. The aliphatic region in the ^{1}H nmr spectrum is also in favor of a 2-3 trans configuration; it was confirmed by the fact that in an NOE difference study of the compound 5 no NOE effect was observed between H-2 and H-3. The lignan 5 is a 5'-methoxypodorhizol. Indeed an acidic cyclization of 5 led to the formation of aryltetrahydronaphtalenes which are identified as hernandin and picrohernandin.[11] However, the formation of a 1-α aryltetrahydronaphtalene by cyclization and the elimination of the absorption at ν 3435 cm^{-1} in the ir spectrum by dilution is in favor of 6 S configuration.

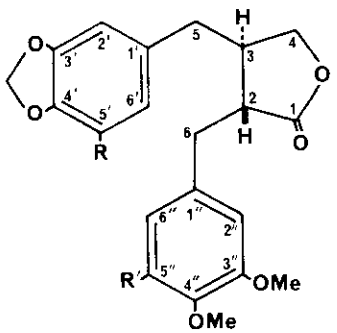
Table 1 : ^{13}C nmr spectra ($CDCl_3$, ppm)

	C-1	C-2	C-3	C-4	C-5	C-6	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'
2	178.3	46.5	41.1	71.1	38.7	35.3	132.3	108.5	149.2	134.0	143.5	102.4
3	178.5	46.5	41.1	71.7	38.4	35.3	131.7	108.8	148.0	146.5	108.3	121.6
4	178.7	46.6	41.1	71.2	38.4	34.7	131.7	108.8	148.0	146.4	108.3	121.6
5	178.2	52.7	36.5	72.7	39.7	72.1	132.2	108.5	149.1	133.9	143.2	102.2
6	178.3	52.7	36.3	72.0	39.3	72.0	131.3	108.4	147.7	146.1	107.8	121.4

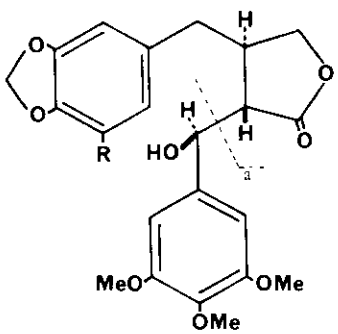
	C-1"	C-2"	C-3"	C-4"	C-5"	C-6"	OMe-3"	OMe-4"	OMe-5"	OMe-5'	$O-CH_2-O$
2	133.3	106.4	153.3	137.1	153.3	106.4	56.2	60.8	56.2	56.8	101.4
3	133.4	106.4	153.3	137	153.3	106.4	56.1	60.8	56.1	-	101.4
4	130.2	111.2*	121.4	149.2	121.4	111.3*	55.4	55.4	-	-	101.1
5	136.5	102.4	153.4	137.5	153.4	102.4	56.2	60.8	56.2	56.8	101.4
6	136.6	102.2	153.2	137.2	153.2	102.2	56.0	60.8	56.0	-	101.1



1



2 R = R′ = OMe
3 R=H R′=OMe
4 R = R′ = H



5 R=OMe
6 R=H (Podorhizol)[12]

REFERENCES AND NOTES

1- Part VII in the serie "Study of Hernandiaceae" (part VI: P. Richomme, M. Lavault, H. Jacquemin and J. Bruneton, Planta medica, 1984, 1 , 20).

2- P. Richomme, M.-M. Debray, P. Cabalion and J. Bruneton, J. Natural Products, in press.

3- A.M. Duffield, J. Heterocyclic Chem., 1967, 4, 16.

4- G. Rucker and B. Langman, Tetrahedron Lett., 1978, 457.

5- J. Harmatha, M. Budezinsky and A. Trka, Coll. Czech. Chem. Comm., 1982, 47, 644.

6- J.E.T. Corrie, G.H. Green, E. Ritchie and W.C. Taylor, Austr. J. Chem., 1970, 23, 133.

7- Spectral data for 2 and 5

2: ir (CCl_4, ν cm^{-1}) 2940-2915, 2840, 1760, 1585, 1500, 1235; ms: m/z 430 (M^+, 91), 265 (5), 238 (3.8), 191 (9), 181 (100), 165 (38.5), 161 (9), 151 (18), 135 (19); ^1H nmr (δ, ppm): 6.36 (s, H-2" and H-6"), 6.17(d,H-2'), 6.15(d, H-6'), 5.94(dd, O-CH_2-O), 4.18(q,H-4b), 3.87(q, H-4a), 3.85(s, OMe-5), 3.83(s, OMe-3" and OMe-5"), 3.82(s, OMe-4"), 2.91(m, H-6a and H-6b), 2.60 (m, H-2), 2.55(m, H-5a and H-5b), 2.48(m, H-3) ($J_{2,6}$: 5.4 Hz, $J_{3,4a}$:7.0 Hz, $J_{3,4b}$: 7.2 Hz, $J_{4a,4b}$: 9.0 Hz, $J_{6a,6b}$: 14 Hz, $J_{2',6'}$: 1.8 Hz, J_{O-CH_2-O}: 5 Hz)

5: α_D: -20.5° ($CHCl_3$, c=1); mp: 112-113°c; ir (KBr, ν cm^{-1}) 3435, 2840, 1750, 1580, 1400, 940; ms: m/z 446 (M^+, 12.8), 197 (100), 181 (35.7), 165 (11.4); ^1H nmr (δ,ppm): 6.50 (s, H-2" and H-6"), 6.01(s, H-5'), 5.95(s, H-2'), 5.91(d, O-CH_2-O), 5.27(d, H-6), 4.37(q, H-4b), 3.96(q, H-4a), 3.82(s, OMe-5' , OMe-3", OMe-4" and OMe-5"), 2.81(m, H-3) 2.63(m, H-2), 2.43(m, H-5b), 2.23(m, H-5a) ($J_{2,3}$: 6 Hz, $J_{2,6}$: 5.7 Hz, $J_{3,4b}$: 7.8 Hz, $J_{4a,4b}$: 8.9 Hz, $J_{5a,5b}$: 13.7 Hz, $J_{5a,3}$: 7.7 Hz, $J_{5b,3}$:7.8 Hz, $J_{2',6'}$: 1.4 Hz, J_{O-CH_2-O} 1.0 Hz).

8- CD (EtOH) $\Delta\varepsilon_{nm}$: 2: -3.5_{239}, -0.9_{278} ; 3: -2.6_{240}, -0.2_{280}; 5: -3.8_{241}, -0.9_{280}

9- Yatein is also present in the plant[2] and has been previously isolated by H. Erdtman and J. Harmatha, Phytochemistry, 1979, 18, 1495; also by S.K. Koul, S.C. Tanaja, K.L. Dhar and C.K. Atal, Phytochemistry, 1983, 22, 999.

10- D. Takaoka, M. Imooka and M.Iroi, Bull. Chem. Soc. Japan, 1977, 50, 2821; S. Nishibe, B. Hisada and I. Inagaki, J. Pharm. Soc. Japan, 1974, 94, 522.

11- H. Yamaguchi, M. Arimoto, K. Tanoguchi, T. Ishida and M. Inoue, Chem. Pharm. Bull., 1982, 30, 3212.

12- M. Kuhn and M. Arimoto, Helv. Chim. Acta, 1967, 50, 1546.

Received, 26th June, 1984