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PIMOLIN, A NEW CLASS OF NATURAL PRODUCT FROM *PIMPINELLA MONOICA*: A NOVEL DIMERIC FUROCHROMONE

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Abstracts: Pimolin (1), a novel dimer of the furochromone, visnagin, has been isolated from the chloroform extracts of the seeds of the plant, *Pimpinella monoica*. Its structure as elucidated by multidimentional ^{1}H and ^{13}C nmr spectroscopy *via.* long range coupling (COLOC and COSYLR), indicated 2+2 pyrone-furan cycloaddition.

The insect antifeedant activity of the extracts of the common ornamental plant, lady's lace, *Pimpinella monoica* Dalz[1] led to a detailed phytochemical investigation resulting in the isolation of several compounds[2]. We report herein the characterisation of a new dimeric compound, *Pimolin* (1), isolated from the $CHCl_3$ extracts of the seeds of the plant.

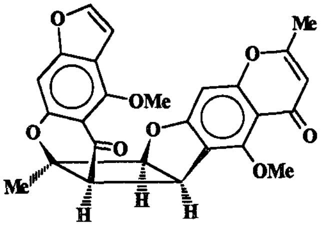
Pimolin, is a colourless crystalline compound analysing for $C_{13}H_{10}O_4$. The IR absorptions at 1675, 1670 cm^{-1} indicated the presence of at least two carbonyl groups. The UV absorptions (252.5, 282.1 and 365.0 nm) showed a similarity to those of furobenzopyrones[2]. Of the twenty protons in the ^{1}H nmr spectrum, the presence of two methyls, two methoxyls, a pair of downfield doublets and three olefinic / aromatic singlets and three sp^3 methine protons were readily discernible. The double doublets appearing at δ 5.21 (J = 2.1, 6.6), 4.50 (J = 6.6, 8.5) and 3.61 (J = 2.1, 8.5) represent an AMX spin system. The doublets at δ 7.38 and 6.70 (J = 1.5 each) could be due to furan protons. The ^{1}H-decoupled ^{13}C nmr spectrum of 1 (see table) indicated the presence of twenty six carbons. The multiplicities of the carbon resonances inferred from the DEPT and gated-decoupled spectra, indicated two methyls, two methoxyls, five sp^2, three sp^3 methines and fourteen quaternary carbons. On the basis of chemical shifts, two quaternary carbons at δ_c 176.4 and δ_c 184.9 could be attributed to carbonyls, seven to O-bonded aromatic or olefinic, four sp^2 and one O-bonded sp^3 carbons.

The nmr data along with the molecular ion peak at 460 in the ms suggested that pimolin could be a dimer of visnagin, $C_{13}H_{10}O_4$ (2). In fact, on treatment of 1 with *p*-toluenesulfonic acid in benzene, two equivalents of 2 were obtained. Presence of two vicinally coupled furan protons, an AMX spin system of three saturated CH suggested that in the formation of 1, fusion between pyrone double bond of one molecule with that of furan of another is involved. Further evidence leading to the structure and stereochemistry of 1 necessitated extensive study by 2D nmr spectroscopy.

Of the three olefinic / aromatic signals, the resonance at δ 5.87 was assigned to 3-H on the basis of its allylic (^{4}J) coupling with 2-CH_3 (δ 2.15) in the ^{1}H-^{1}H COSYLR spectrum. The singlet at δ 6.72 displayed long range coupling with 6'-H and was due to 9'-H. Therefore the remaining methine singlet at δ 5.98 was assigned to 9-H. The presence of an AMX spin system was further confirmed by the following COSYLR interactions: (δ_H-δ_H); (3.61 <---> 4.50), (3.61 <---> 5.21) and (4.50 <---> 5.21). Of these, the signal at δ 4.50 was ascribed to 6-H on the basis of it's COSYLR interaction with 9-H. Therefore, the proton at δ 5.21 is assigned to 7-H (O-bonded), whereas the other proton of the AMX spin system (δ 3.61) was assigned to 3'-H. The magnitudes of the *vicinal* couplings between 3'-H and 6-H (J = 8.5 Hz, $\Phi_{cacl.}$ = 0°) and between 6-H and 7-H (J = 6.6 Hz, $\Phi_{cacl.}$ = 25.5°) suggested that these protons could be cis-disposed.

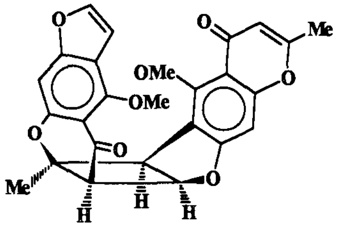
The methoxyl at δ 3.67 showed an nOe with the 6'-H and therefore was located at the C-5' position. In the ^{13}C-^{1}H HETCOR spectrum, all the expected CH-cross peaks through $^{1}J_{CH}$ were observed including those for the cyclobutane moiety at (δ_C-δ_H): (40.7<---> 4.50) at C-6; (90.7 <---> 5.21) at C-7 and (57.0 <---> 3.61) at C-3'. Based on these spectroscopic data structures **1** and **1a** could be proposed. Unequivocal assignments of quaternary carbons and the differentiation between **1** and **1a** could be achieved by COLOC[4,5].

The salient features of the COLOC spectrum were: i> the carbonyl carbon at δ 189.1 showed coupling with 3'-H and was therefore assigned to C-4'. C-4' showed additional COLOC interaction with 6-H. Such a situation exists only in structure **1** and not in **1a**. The other carbonyl at δ 176.4 was therefore at C-4 position. iii> The quaternary carbon at δ 78.7 showed cross peaks with the 2'-Me protons and 6-H, hence was assigned to C-2'. iv> C-7 displayed a COLOC interaction with the 2'-Me protons. This further ruled out structure **1a** where such a C-H coupling is improbable. v> In addition to this, the unequivocal assignments of the carbons C-2, C-5 and 5', C-8a and 8a", C-9a and 9a' (7C, δ 153.9 - 166.2) and also those of C-4a and 4a' and C-5a and 5a" (4C, δ 110.4 - 113.7) which appear in a narrow range in the 1D spectrum, were possible from the COLOC spectrum. Thus, all the carbon resonances could also be assigned unequivocally. Based on these data, the structure of pimolin was unequivocally was established as **1**.

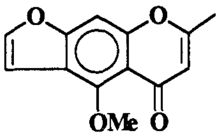


(1)

Pimolin



(1a)



(2)

Visnagin

The stereochemistry of **1** could be derived from the spatial disposition of the cyclobutane protons 6-H, 7-H and 3'-H with respect to 2'-Me from a phase sensitive 2D nOe (NOESYPH) spectrum[5]. Significant nOe were observed between 2'-Me <---> 3'-H, 2'-Me <---> 7-H, 6-H <---> 7-H and 6-H <---> 3'-H. These observations could only be explained if the 6-H, 7-H and 3'-H were *cis*-disposed with respect to 2'-Me group. Therefore, in the formation **1**, 2+2 furan-pyrone cycloaddition is postulated.

To the best of our knowledge, pimolin represents the first dimeric natural product of its kind. In the energy minimised models[6] of **1**, the two pyranobenzofuran moieties were *cis* disposed resulting in the formation of an intramolecular cavity between these two moieties. With eight oxygen atoms in the molecule, it could be a potential candidate as a host molecule. This fact was also indirectly corroborated from the solvent induced ^{1}H nmr shifts. In C_6D_6, all the protons of the cyclobutane ring shifted upfield (~0.6 ppm) possibly due to anisotropic shielding by the guest molecule. The downfield shifts of the C-9' proton and the methoxyl protons at C-5 suggests that the benzene is lodged laterally in the cavity, parallel to the cyclobutane ring and situated in a plane passing through the C-5 and C-9' carbons.

Table 1. 1D and 2D NMR data of pimolin, 1 in $CDCl_3$

Pos.	δ^{13}_C	DEPT	δ_H (J=Hz)	COSYLR[@]	COLOC (C-->H)	NOESY
2	162.8	-C-			2-Me	
2-Me	19.5	$-CH_3$	2.15 (d, 0.5)	3-H		3-H
3	111.3	-CH	5.87 (d, 0.5)	2-Me	2-Me	2-Me
4	176.4	-C=O				
4a	111.7	-C-			3-H	
5	157.4	-C-			5-OMe	
5-OMe	61.5	$-CH_3$	4.0 (s)			
5a	113.9	-C-			6-H, 9-H	
6	40.6	-CH	4.50 (dd,6.6,8.5)	7-H,3'-H		7-H,3'-H
7	90.5	-CH	5.21 (dd,6.6,2.1)	6-H,3'-H	2-Me	2-Me,6-H
8a	166.8	-C-			6-H,7-H	
9	92.9	-CH	5.98 (s)	6-H		
9a	160.2	-C-			9-H	
2'	78.7	-C-			2'-Me,6-H	
2'-Me	25.8	$-CH_3$	1.69 (bs)			3'-H,7-H
3'	57.0	-CH	3.61 (dd, 2.1,8.5)	6-H.7-H	2'-Me,7-H	6-H,2'-Me
4'	189.1	-C=O			3'-H,6-H	
4'a	110.4	-C-			9'-H	
5'	153.9	-C-			5'-OMe	
5'-OMe	60.2	$-CH_3$	3.67 (s)			6'-H
5'a	112.6	-C-			6'-H,7'-H	
6'	105.4	-CH	6.70 (d, 1.5)	7'-H,9'-H		7'-H,5'-OMe
7'	143.5	-CH	7.38 (d, 1.5)	6'-H		6'-H
8'a	159.9	-C-			6'-H,7'-H	
9'	94.5	-CH	6.72 (s)	6'-H		
9'a	159.5	-C-			9'-H	

[@] includes COSY peaks

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2. Luthria, D. L.; Prabhu, B. R.; Banerji, A.; unpublished results.
3. Crystallised solids from hot methanol, Mp 240^0, Empirical Formula: $C_{13}H_{10}O_4$; $[\alpha]^{28}$ -15.1^0(c, 0.528 in $CHCl_3$); IR^{KBr}: 1675, 1670, 1620, 1585, 1480, 1180 cm^{-1}; UV^{MeOH} nm (log ϵ); 252.5 (4.13), 282.1 (3.82), 365.0 (2.51); MS m/z (rel. int.): 460, 231, 230 (91.7%), 201 (100%), 184 and 160.
4. ^1H and ^{13}C nmr were recorded on a Bruker AC-200 spectrometer operating at 200.13 and 50.33 MHz, respectively. In COLOC, 512 transients were recorded with 100 t_1 increments. he delay parameters were; d_1 = 2 sec., d_3 = 0.032 sec. and d_4 = 0.016 sec. using the pulse sequence of Kessler *et al.*[5] For NOESYPH experiment a mixing time of 0.9 sec was used.
5. Kessler, H.; Griesinger, C.; Zarbok, J; Loosli, H. R.; *J. Mag. Reson.*, **57**, 331 (1984)
6. Desktop Molecular Modeller (version 1.0), Oxford Electronic Publishing, OUP, Walton street, Oxford, U. K, was utilised for molecular modeling.

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