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REVISED STRUCTURES FOR EPIASCHANTIN AND EPIMAGNOLIN

By, Andrew Pelter* and Robert S. Ward

Department of Chemistry, University College of Swansea, Singleton Park, Swansea, SA2 8PP, U.K.

and Chikao Nishino

Mitsubishi-Kasei Institute of Life Sciences, 11, Minamiooya, Machida-Shi, Tokyo, Japan

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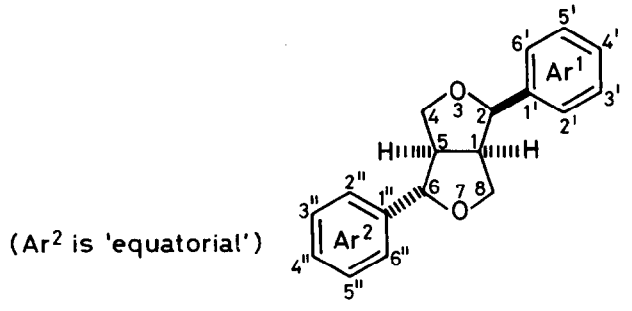
Summary ^{13}C-Chemical shifts confirm the nature of the aryl groups of epiaschantin and epimagnolin. They also allow the configurations assigned to these compounds to be corrected and yield general criteria for the assignment of stereochemistry to similar lignans.

The question of assignment of configuration to the aryl groups of the epi-series of 2,6-diaryl-3,7-dioxabicyclo[3,3,0]octanes (1) ($Ar^1 \neq Ar^2$) is a difficult one for which until recently[1] no general solution has been proposed.



(1)

	Ar^1	Ar^2
(a)	veratryl*	piperonyl*
(b)	piperonyl	veratryl
(c)	piperonyl	3,4,5-trimethoxyphenyl
(d)	veratryl	3,4,5-trimethoxyphenyl
(e)	3,4,5-trimethoxyphenyl	piperonyl
(f)	3,4,5-trimethoxyphenyl	veratryl

* veratryl = 3,4-dimethoxyphenyl, piperonyl = 3,4-methylenedioxyphenyl

Attempts to solve the structural problems presented have depended on some method for associating the ^{1}H n.m.r. signals of the benzylic protons at C-2 and C-6 with specific aryl groups, followed by application of the Karplus equation in order to assign the stereochemistry of these protons and hence of Ar^{1} and Ar^{2}. The most general approach was an attempt to use europium shift reagents as a means for deciding which benzylic proton is close to a particular aryl ring.[2] However, this approach fails as the shifts observed are a complex function of the substituents and stereochemistry of any aryl ring.[1] Furthermore the Karplus equation cannot be applied in this series[1,3,4,5] and attempts to use it have resulted in incorrect stereochemical assignments.[1] Thus the high field benzylic proton, characteristic of the epi-series only and not observed in the parent diequatorial or dia-series, was assigned to an equatorial proton,[2] whereas it has now been unequivocally shown to be diagnostic of an axial benzylic proton.[1] ^{1}H N.m.r. criteria alone therefore offer no general methods for the determination of the stereochemistry of these lignans.

We have recently shown[1] that the structures of lignans such as methyl pluviatilol (1a) and methyl xanthoxylol (1b) can be unambiguously assigned on the basis of their ^{13}C n.m.r. spectra. In particular the chemical shifts of the 1' and 1'' carbon atoms are sensitive in a consistent fashion to changes in the substituents on the aromatic rings and to their stereochemistry. The chemical shifts of the 2,6- and 1,5- and 4,8-carbon atoms are also sensitive to stereochemistry but not to changes in the aryl groups. We have now examined the ^{13}C n.m.r. of epiaschantin and epimagnolin, previously assigned structures (1c) and (1d)[2] and propose that the structures be revised to (1e) and (1f) respectively.

The ^{13}C n.m.r. spectra of the two compounds (Table 1) completely confirm that they belong to the unsymmetrical epi-series of 2,6-diaryl-3,7-dioxabicyclo[3,3,0]-octanes and also confirm the nature of the aryl groups associated with each compound.

Examination of the 1',1''-chemical shifts (Table 2) shows that the compounds have 3,4,5-trimethoxyphenyl groups in extremely similar environments, as previously proposed, but that these groups cannot be equatorial as otherwise the signal would appear at ca. 136.6 p.p.m. This is confirmed in that the veratryl group of epimagnolin must be equatorial (ca. 135.5 p.p.m.) rather than axial (ca. 130.8 p.p.m.). Similarly the 1''-carbon atom of the piperonyl group of epiaschantin appears in precisely the region expected for an equatorial piperonyl group of an epi-lignan and is well removed from the region expected for an axial piperonyl group. Thus the structures of epiaschantin and epimagnolin are unequivocally (1e) and (1f), and the chemical shift for C-1 of an axial 3,4,5-trimethoxyphenyl group of this series of lignans is ca. 134.15 p.p.m. We also include in Table 2 information obtained by examination of pinoresinol and epipinoresinol relating to the 4-hydroxy-3-methoxyphenyl group.[6]

Table 2 gives information that should allow ready assignment of structure to almost all of the naturally occurring bicyclic lignans of the type discussed. Compounds containing free phenolic groups are readily O-methylated for comparison purposes. It is interesting to note that when any of the aryl groups in the epi-series moves from equatorial to axial there is an average shift upfield of 2.5 - 2.7 p.p.m. in the signal due to C-1'. In cases for which other data are not available, this trend may be useful for structural purposes.

Table 1 ^{13}C N.M.R. Spectra[x]

Carbon	Epiaschantin	Epimagnolin
1	50.15	50.15
5	54.58	54.46
4	71.07	71.08
8	69.76	69.74
2	82.23	82.25
6	87.69	87.65
1'	134.13	134.16
2'6'	102.76	102.77
3'5'	153.31	153.30
4'	137.10	137.09
1''	135.21	133.75
2''	106.56	109.32
5''	108.19	111.21
3''	147.28	148.84
4''	148.04	149.35
6''	119.55	118.50
OMe	60.88	60.86
	56.21	56.20
		55.96
OCH_2O	101.07	-

[x] All values given as p.p.m. downfield from TMS. All spectra run in $CDCl_3$. All assignments supported by off-resonance decoupling experiments.

Table 2

^{13}C N.M.R. chemical shifts of 1' and 1" carbon atoms of 2,6-diaryl-3,7-dioxabicyclo[3,3,0]octanes

Equatorial veratryl	δ^{*}(1',1")	Axial veratryl	δ(1',1")
Eudesmin	134.04	Diaeudesmin	131.38
Methyl piperitol	133.38	Methyl pluviatilol	130.86
Epieudesmin	133.51	Epieudesmin	130.81
Epimagnolin	133.75		
Equatorial piperonyl		**Axial piperonyl**	
Sesamin	134.93		
Methyl piperitol	134.94		
Aschantin	134.93		
Episesamin	135.63	Episesamin	132.65
Methyl pluviatilol	135.08		
Epiaschantin	135.21		
Equatorial 3,4,5-trimethoxyphenyl		**Axial 3,4,5-trimethoxyphenyl**	
Aschantin	136.67	Epiaschantin	134.13
Yangambin	136.64	Epimagnolin	134.16
Equatorial 4-hydroxy-3-methoxyphenyl		**Axial 4-hydroxy-3-methoxyphenyl**	
Pinoresinol	132.95		
Epipinoresinol	133.09	Epipinoresinol	130.36

* All values given in p.p.m. downfield from TMS

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