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PRAECANSONE A: EVIDENCE FOR THE EXISTENCE OF 8,9-(E) AND 8,9-(Z) ISOMERS IN EXTRACTS FROM *TEPHROSIA PUMILA*

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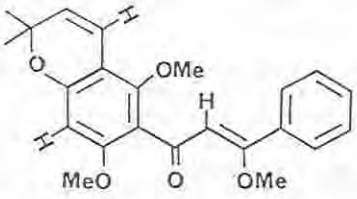
ABSTRACT. The structure of praecansone A was recently revised from **1** to **2** on the basis of NMR (^1H, ^{13}C, nOe) and EIMS data. We now wish to report the isolation of two geometrical isomers of praecansone A from an extract of the seed-pods of *Tephrosia pumila* and present evidence that the initial isolate is the 8,9-(Z) form (**2**) which converts on standing into the 8,9-(E) form (**3**). It is (**3**) rather than (**2**) which represents the compound described previously as praecansone A.

INTRODUCTION

Praecansone A was first isolated from *Tephrosia praecans* (1) and assigned structure (**1**). Pelter et al. (2) commented that the evidence presented was more appropriate for the 7-oxo form and the revision, on the basis of spectroscopic data, of the structure of praecansone A to 7-oxo-9-methoxy chalcone (**2**) has been published (3). In a recent investigation (4) of the seed-pods of *Tephrosia pumila* (Lam.) Pers. we reported the occurrence of praecansone A as the major flavonoid. In a further study of the same species (5) we were able, by circular preparative TLC, to isolate, in addition to praecansone A, a labile isomeric chalcone which, in chloroform solution, gradually converts into the geometric isomer with the spectral characteristics recorded previously for praecansone A (1, 3, 4).



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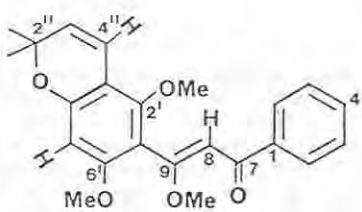

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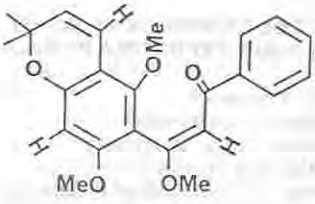

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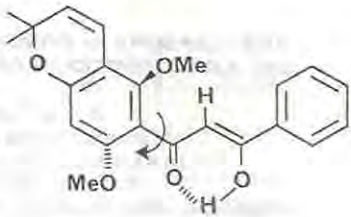

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MATERIALS AND METHODS

Plant material. Pods of *Tephrosia pumila* were collected from Gibey Valley, Ethiopia, in September 1987. Collection details have already been published (5).

Spectroscopy. ^1H NMR and nOe spectra were recorded on a Bruker WH-360 spectrometer using $CDCl_3$ as solvent.

Extraction. Ground pods (1 kg) were extracted by percolation with petrol (b.p. 60-80°C) for 3 days and then with $CHCl_3$ for 5 days. Evaporation of the petrol yielded an oily residue which was taken up in Me_2CO and filtered. CC of the Me_2CO-soluble fraction was performed on silica gel (100 g) eluting with petrol: EtOAc mixtures of increasing polarity. Forty 100 ml frs were collected. Frs 10/20 (5% EtOAc) gave pumilaisoflavone A (4) (7 mg); frs 21/30 (10% EtOAc) contained a mixture which was separated by circular preparative TLC (solvent, petrol: benzene: EtOAc 3:2:1) to give **3** (300 mg, λ_{max} (MeOH) 231, 236sh, 276 nm) and **2** (24 mg, λ_{max} (MeOH) 229, 235sh, 288, 295sh nm). Frs 31/40 (15% EtOAc) gave pumilaisoflavone B (4) (16 mg).

RESULTS AND DISCUSSION

Analyses of the ^1H and ^{13}C NMR spectra of the two isomers indicate that praecansone A is actually represented by structure (**3**), where the 8,9-double bond is in the (E)-configuration, while the transient isomer is represented by the structure previously assigned to praecansone A (e.g. **2**), in which the 8,9-double bond is in the (Z)-configuration.

In their formulation of praecansone-A as (**2**) Venkataratnam et. al. (3) reported an nOe experiment in which irradiation of the 9-methoxyl resonance led to a 15% enhancement of H-8. Given the structure they assigned such an nOe appears highly improbable as H-8 will lie *trans* across the 8,9-double bond from that methoxyl. Their result conforms more appropriately with the isomer (**3**) in which a large nOe would be anticipated between the 9-methoxyl and H-8. In the course of this investigation we were able to perform nOe studies on both isomers. The results of these are shown in Table 1 and complete ^1H NMR and ^{13}C NMR data are reported in Table 2. In both isomers H-8 can be differentiated from H-5' by the occurrence of long-range coupling between the latter and H-4".

The stable (major) isomer isolated gave NMR data comparable to that reported previously for praecansone A (3, 4). The nOe study showed clear strong interactions between the three methoxyl resonances and protons lying either

ortho or *peri* to them (e.g., 9-methoxyl with H-8 (as previously reported (3)), 6'-methoxyl with H-5 and 2'-methoxyl with H-4"). By contrast, in the unstable

Table 1. ^{1}H NMR nOe experiments for praecansone A isomers.

Irradiated methoxyl	Enhanced resonances (%) 2	3
2'	H-4" (6) H-8 (3)	H-4" (6)
6'	H-5' (21)	H-5' (18)
9	nil	H-8 (21)

Table 2. ^{1}H and ^{13}C NMR chemical shift data for praecansone A isomers.

	2		3	
	^{1}H	^{13}C	^{1}H	^{13}C
C-1	-	140.2	-	139.9
C-2/6	7.95 m	128.1[a]	7.81 m	127.8[a]
C-3/5	7.43 m	128.0[a]	7.36 m	127.6[a]
C-4	7.43 m	131.5	7.36 m	131.2
C-7	-	188.9	-	189.9
C-8	6.05 s	105.1	6.40 s	101.4
C-9	-	163.7	-	165.7
C-1'	-	107.8[b]	-	107.5[b]
C-2'	-	158.4[c]	-	157.7[c]
C-3'	-	109.8[b]	-	111.5[b]
C-4'	-	155.0[c]	-	154.6[c]
C-5'	6.24 d (0.8)	95.8	6.13 d (0.8)	96.0
C-6'	-	156.1[c]	-	155.6[c]
C-2"	-	77.0	-	76.3
C-3"	5.55 d (9.9)	116.6	5.43 d (9.9)	116.7
C-4"	6.53 dd (9.9, 0.8)	127.6	6.45 dd (9.9, 0.8)	126.7
2"-Me$_2$	1.45 s	28.0	1.39 s	27.8
2'-OMe	3.79 s	62.0	3.70 s	61.9
6'-OMe	3.78 s	55.8	3.64 s	55.8[d]
9-OMe	3.66 s	57.2	3.85 s	55.6[d]

[a,b,c,d] assignments interchangeable.

(minor) isomer, while the 6'-methoxyl continued to show a strong interaction with H-5', the 2'-methoxyl now gave an interaction with H-8 as well as with H-4" but the 9-methoxyl exhibited no interactions at all. These observations require that in the minor isomer H-8 and the 9-methoxyl substituent must be *trans* to one another with H-8 facing toward the 2'-methoxyl (**2**) while in the preferred isomer H-8 and the 9-methoxyl are *cis* (**3**).

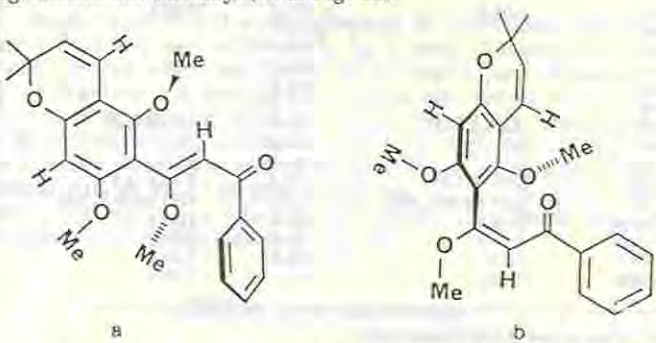
This argument receives support from other NMR studies (Table 1) which may also throw some light on the conformations taken up by the two isomers in solution.

a) In the ^{13}C NMR spectra of (**2**) and (**3**) the resonance for the 2'-methoxyl group is consistently deshielded due to the presence of two adjacent ring substituents which force it to lie out of the plane of the aromatic ring. By contrast, the 6'-methoxyl substituent resonance is shielded because it can lie toward H-5, in the plane of the aromatic nucleus. The third (C-9) methoxyl substituent, shows an appreciable change in resonance, being deshielded by 1.2 ppm in (**2**) in comparison to (**3**). This deshielding must be attributed to the methoxyl being forced to lie away from the plane of the 8,9-double bond and would be expected only in the (Z)-isomer (**2**).

b) In the ^{1}H NMR spectra individual methoxyl resonances can be assigned unambiguously from the results of the nOe experiments. There are marked

changes in the chemical shifts of the 6'- and 9-methoxyl resonances between (**2**) and (**3**). In (**2**) the 9-methoxyl is shielded, occurring at δ 3.66. This shielding can be attributed to (**2**) taking up the conformation depicted in Fig. 1a, in which it lies within the shielding cone of the benzoyl moiety, a conformation that is possible if H-8 and the C-7 benzoyl carbonyl are *cis* with the 8,9-double bond and carbonyl remaining planar with the benzopyran system. In (**3**) it is the 6'-methoxyl (and to a lesser extent H-5' and the 2'-methoxyl) groups that are shielded. This can be caused by the 8,9-double bond lying perpendicular to the benzopyran system but planar with the benzoyl moiety, in which case shielding of all three groups would be attributable to the anisotropic effects of the now perpendicularly oriented carbonyl (as depicted in Fig. 1b). This hypothesis receives further support from the UV spectra of (**2**) and (**3**) in which there is a reduction of 12 nm in the position of the major maximum in the transition from (**2**), where the linear chromophore includes the benzopyran nucleus, 8,9-double bond and 7-carbonyl, to (**3**) where conjugation is disrupted between the benzopyran system and the 8,9-double bond.

c) In the ^{1}H NMR spctrum of (**2**) H-8 is shielded by 0.35 ppm in comparison with H-8 in (**3**) (Table 2). The reason for the more shielded environment is probably the sum of the effects of the shift in the 9-substituent from a *cis* to a *trans* relationship and, more significantly, because in (**2**) H-8 will fall within the shielding cone of the carbonyl (as in Fig. 1a).



a b

Fig. 1. Stereochemical representations of the 8,9-(Z) (a) and 8,9-(Z) (b) isomers of praecansone A.

The preferred configuration of praecansone A, in which H-8 is *cis* to the 9-methoxyl (**3**, Fig. 1b), is unusual among chalcones, which generally occur with the *trans* configuration, as seen in praecansone B (**4**) (3) and numerous other chalcones (6). We suspect that the isomer **3** is preferred in praecansone A as it reduces the interaction between the 9-methoxyl and the 7-carbonyl and the other two methoxyl substituents, particularly if the benzopyran substituent also lies perpendicular to the C_6-C_3 substituent. It is noteworthy that Venkataratnam et. al. (3) suggest that in (**4**) the preferred configuration is also one in which the benzopyran lies perpendicular to the C_6-C_3 system, presumably to reduce interaction between the 2'- and 6'-methoxyls and the substituents of the C_3 unit.

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