THE COUMARIN FROM EKEBERGIA SENEGALENSIS: A REVISION

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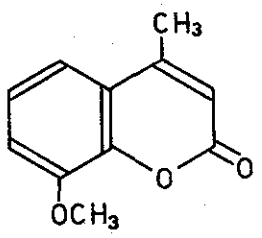
The structure of the coumarin from E.senegalensis is revised to 4-methoxy-5-methylcoumarin (II).

Bevan and Ekong[1] isolated from the heartwood of Ekebergia senegalensis A.Juss (family Meliaceae) a new coumarin, m.p. 165°, to which they attributed the structure of 4-methyl-8-methoxycoumarin (I). However, their statement seems to rest on not unequivocal results. Moreover, they claimed to have synthesized in low yield a product identified with the natural coumarin solely on the basis of its R_f values on TLC: neither the m.p. nor spectral data were reported for the synthetic product.

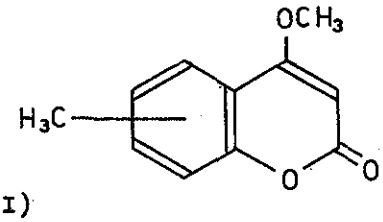
Recently[2] we had the opportunity of suggesting an interpretation of the NMR spectra that allows to distinguish between 4-methyl- and 4-methoxycoumarins. After our results, structure (I) was untenable for the coumarin from E.senegalensis. In fact, the lack of allylic coupling between H-3 and the methyl group, and the reported chemical shift of H-3 (5.65 δ) were not consistent with (I) and pointed to a 4-methoxycoumarin structure.

A first support to our hypothesis came from the synthesis of (I) through a different pathway. Condensation[3] of ethyl acetoacetate with pyrocatechol gave 4-methyl-8-hydroxycoumarin, m.p. 188°-190° (from methanol, in very low yield; treatment with dimethyl sulphate and potassium carbo-

nate in acetone yielded (I), m.p. 137°–138° (from methanol), quite different from the natural coumarin described by Bevan and Ekong. In particular, the NMR spectrum of (I) showed the allylic coupling and the downfield shift of H-3 (6.26 δ) required by this structure.



(I)



(II) 5-CH_3
(III) 6-CH_3
(IV) 7-CH_3
(V) 8-CH_3

The NMR spectra of some coumarins[4,5] report the chemical shift of Ar-CH_3 at 2.28–2.40 δ when the methyl group is on C-6, C-7 or C-8: the few cases we know for 5-CH_3 when OCH_3 or other OR groups are on C-4 are kotanin[6] (5-CH_3 at 2.73 δ), siderin[2] (5-CH_3 at 2.62 δ) and some products reported by Bohlmann[7] (5-CH_3 at 2.52–2.62 δ). Inversely, a 4-CH_3 is shifted to 2.46–2.57 δ by a 5-OCH_3 group[4,5,8]. Therefore, the 2.68 δ value reported by Bevan and Ekong could be interpreted as showing the occurrence of the methyl group on C-5.

None of the four isomeric coumarins (II), (III), (IV) and (V) was known; therefore we prepared all these products.

Condensation of p-cresol with malonic acid in the presence of zinc chloride and phosphorus oxychloride, following the general procedure of Shah[9], gave 4-hydroxy-6-methylcoumarin, m.p. 245°–246° (from acetic acid), lit.[10] 247°; treatment with dimethyl sulphate and potassium carbonate in acetone[2] yielded (III), m.p. 125°–126° (from cyclohexane).

The same condensation performed on o-cresol afforded 4-hydroxy-8-methylcoumarin, m.p. 229°–230° (from ethyl acetate), lit.[11] 231°–232°, that was methylated to (V), m.p. 147°–148° (from methanol).

The condensation on m-cresol yielded a mixture, that was resolved by fractional crystallization from methanol. 4-Hydroxy-7-methylcoumarin, less soluble, has m.p. 207°–208° (from methanol), lit.[11] 216°–

-217°: by methylation it gave (IV), m.p. 156°-157° (from methanol). 4-Hydroxy-5-methylcoumarin, more soluble and obtained in poor yield, has m.p. 232°-233° (from aqueous ethanol), lit.[11] 233°-234°; by methylation it gave (II), m.p. 162°-163° (from cyclohexane).

Direct comparison of the NMR spectra (see Table) proved that 4-methoxy-5-methylcoumarin (II) has the identical data reported for the natural product. Hence the coumarin extracted from E.senegalensis has the revised structure (II).

The interpretation of NMR spectra reported in this and in the previous paper[2] will help in the elucidation of the structures of natural coumarins.

All the products reported in this paper gave satisfactory elemental analyses.

Table

	H-3	OCH_3	$Ar-CH_3$	H-5	H-6	H-7	H-8
Bevan and Ekong	5.65	3.95	2.68	—	——6.95-7.53——		
synthetic (I)	6.26q	3.92	2.39d	——7.05-7.25——			—
synthetic (II)	5.62	3.92	2.65	—	——6.90-7.35——		
synthetic (III)	5.63	3.96	2.39	7.55	—	7.30d	7.09d
synthetic (IV)	5.62	3.97	2.43	7.66d	7.02d	—	7.08
synthetic (V)	5.64	3.94	2.41	7.61dd	7.07t	7.34dd	—

-if not otherwise indicated, all signals are singlet

-solvent: $CDCl_3$ for (I-V); not reported for the natural coumarin

-(I): J_{allyl} 1.2 Hz. (III): $J_{7,8}$ 8.5 Hz. (IV): $J_{5,6}$ 8 Hz. (V): $J_{5,6}$ 8 Hz, $J_{6,7}$ 8 Hz, $J_{5,7}$ 2 Hz.

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