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STRUCTURE OF NUCLEAR C-METHYLATED CHROMONES[x]

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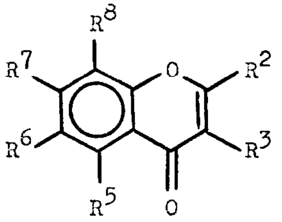
The nuclear methylation of the A ring of flavonoids is known. Little data are available, however, for the anologue reaction of hydroxybenzopyrones (chromones)[1,2,3]. In this work 2,3-dialkyl-5,7-dihydroxy-chromones (Ia-d) were converted into 8-C-methyl derivatives by boiling them in methanol in the presence of methyliodide and sodiummethoxide. The structures of the 7-methoxy-8-C-methyl derivatives (IIa-d) thus obtained were established by means of NMR spectroscopy. The NMR spectra of Ia-d and IIa-d resp., were compared with those of the 7-methoxy (III), 5-acetoxy-7-methoxy (IV) derivatives of I, and with those of the 5-acetoxy derivatives of II (V), respectively. In each case independently of the 2,3-alkyl groups, the same type of compound (II) was obtained. The clarification of the structure is demonstrated with compound IIa. All data for the remaining models are very similar.



R^2 = Me (a,b); Et (c,d)
R^3 = Me (a,c); Et (b,d)
R^5 = OH (I-III), OAc (IV,V)
R^6 = H ; R^7 = OH (I), OMe (II-V)
R^8 = H (I,III,IV); Me (II,V)

In the NMR spectrum of IIa there are 6 singlets at δ=1.90, 2.01, 2.27, 3.82, 6.13 and ~ 13.0 ppm., the intensity of which correspond to 3, 3, 3, 3, 1 and

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1 proton, resp. The first three peaks correspond to protons of methyl groups on an aromatic ring, the 3.82 ppm signal to a methoxy group. The next two can be assigned to an aromatic and to a chelated hydroxy proton, resp. Thus an additional nuclear methyl group appeared in the molecule in addition to that due to the methylation of the 7-hydroxy group. The position of this group (6 or 8) must be determined. Since the chemical shifts of H-6 and H-8 protons are very similar (the difference is ~ 0.1 ppm) the problem cannot be solved by the chemical shift of the remaining aromatic proton. By comparing the appropriate chemical shift differences of the aromatic proton in compounds II and those in the acetoxy derivatives of V the determination of the position of the nuclear methyl group is made possible : in the case of the 6-CMe; 8-CH isomer the acylation of 5-C-OH should result in a 0.2 ppm paramagnetic shift of the aromatic proton, whereas this shift should be greater than 0.6 ppm in the case of the 6-CH; 8-CMe isomer[4,5].

	δR^6			$\delta R^6, \delta R^8$	δR^8			$\Delta\delta H^6$ in II and V	$\Delta\delta H^6$	$\Delta\delta H^8$
	II	IV	V	III	II	IV	V		in III and IV	
a	6.13	6.72	6.63	6.29	2.01	6.58	2.07	0.50	0.43	0.29
b	6.23	6.72	6.68	6.34	2.07	6.56	2.08	0.45	0.38	0.22
c	6.23	6.75	6.70	6.34	2.05	6.58	2.10	0.47	0.41	0.24
d	6.24	6.75	6.70	6.30	2.05	6.58	2.10	0.46	0.45	0.28

The measured shift between 0.50-0.45 ppm suggests a 8-CMe pattern. Latter has been further supported by the NMR spectra of compounds III-IV in which the differences of the chemical shifts between 8-CH and 6-CH were found in the region of 0.22-0.29 and 0.38-0.45 ppm, resp., (Table).

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