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SYNTHESIS OF CARPACHROMENE

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Acacetin (4) on reaction with prenyl bromide in the presence of methanolic sodium methoxide yielded 6,8-di-C,C-prenyl-(5) and 6-C-prenyl-(9) derivatives. DDQ reaction with 9 followed by methylation afforded di-O-methyl carpachromene (2). Nuclear prenylation of apigenin (3) gave 6,8-di-C,C-prenyl-(15) and its 7-prenyl ether (14) and 6-C-prenyl-(16) derivatives. DDQ reaction of 16 provided natural carpachromene.[2] The structure of the isopentenylated apigenin isolated by Dreyer et al.[3] requires re-examination.

Two natural compounds have been assigned the same constitution as 5,4'-dihydroxy-6",6"-dimethylpyrano(2",3":7,6)flavone (1); one is carpachromene (m.p. 239-41°; diacetate m.p. 239-41°) isolated from the leaves of Flindersia leavicarpa[2] and the other one (m.p. 276-78°; diacetate m.p. 216-19°) was isolated from the foliage of Pamburus missionis.[3] However, their m.p.'s and some spectroscopic data (see Tables 1,2 and 3) do not agree. The present unambiguous synthesis of 1 and its dimethyl ether (2) shows that carpachromene has this structure (1). Hence the other natural product may have a different structure.

Acacetin (4) when reacted with prenyl bromide in the presence of methanolic sodium methoxide yielded two compounds. The major product was identified as 6,8-di-C,C-prenyl derivative[4] (5), m.p. 200-1°; R_F 0.65 (solvent B)[5] dark brown ferric reaction. In accordance with this structure, it formed diacetate (6) m.p. 190-91°; R_F 0.5 (solvent C) whose NMR spectrum (see Table 3) showed the expected signals. Further it gave a monomethyl ether (7), m.p. 146°; R_F 0.8 (solvent B); and a bisdihydropyran derivative (8), m.p. 199-200°; R_F 0.4 (solvent C).

The second minor fraction in the above reaction was identified as 6-C-prenyl acacetin (9); m.p. 221-22°; R_F 0.5 (solvent B); brown ferric reaction.

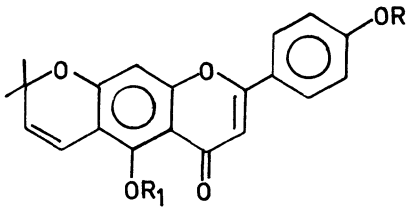
The presence of one C-prenyl unit and two free hydroxyls were indicated by the formation of diacetate (10), m.p. 164-65°; R_F 0.41 (solvent C); having the expected NMR data (see Table 3). Selective methylation of the non-chelated hydroxyl group in compound (9) with one molecular equivalent of Me_2SO_4 yielded its 7-methyl ether (11), m.p. 166-67°; R_F 0.80 (solvent B); NMR (see Table 3).

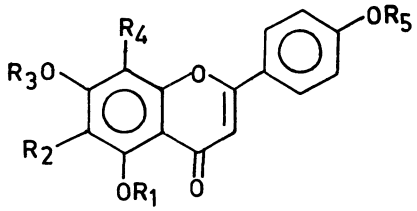
Table 1: UV data[6]

Natural carpachromene	234 (4.48), 300sh (4.49), 308 (4.50) and 344 (4.44)
Natural pyranoflavone from P. Missionis (in EtOH)	236, 273, 279, 313, 330 and 355 nm
Synthetic 1	235 (4.42), 310 (4.50) and 332 nm (4.41)
Diacetate of natural carpachromene	222 (4.51), 265 (4.46) and 317 nm (4.35)
Diacetate of natural pyranoflavone from P. Missionis	228, 283 and 322 nm
Synthetic diacetate (17)	2 20 (4.40), 263 (4.39) and 314 nm (4.32)
Dimethyl ether of natural carpachromene	225 (4.52), 267 (4.37) and 327 nm (4.47)
Synthetic dimethyl ether 2	223 (4.50), 264 (4.20) and 312 nm (4.25)

Table 2: Mass Fragments

Natural carpachromene	336(39%), 335(7), 323(5), 322(32), 321(100), 307(5), 203(18), 161(5), 160(11), 69(7)
Natural pyranoflavone from P. Missionis	336(18), 322(20), 321(100), 203(45), 18(20).

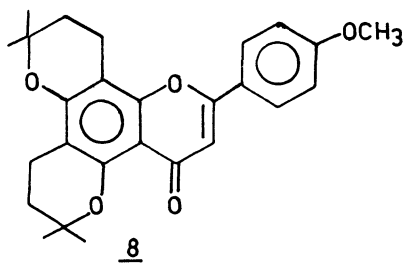




1, R = R_1 = H; Carpachromene
2, R = R_1 = Me
13, R = Me, R_1 = H
17, R = R_1 = Ac

3, R_1 = R_2 = R_3 = R_4 = R_5 = H
4, R_1 = R_2 = R_3 = R_4 = H, R_5 = Me
5, R_1 = R_3 = H, R_2 = R_4 = Pren, R_5 = Me
6, R_1 = R_3 = Ac, R_2 = R_4 = Pren, R_5 = Me
7, R_1 = H, R_2 = R_4 = Pren, R_3 = R_5 = Me
9, R_1 = R_3 = R_4 = H, R_2 = Pren, R_5 = Me
10, R_1 = R_3 = OAc, R_2 = Pren, R_4 = H, R_5 = Me
11, R_1 = R_4 = H, R_2 = Pren, R_3 = R_5 = Me
14, R_1 = R_5 = H, R_2 = R_3 = R_4 = Pren
15, R_1 = R_3 = R_5 = H, R_2 = R_4 = Pren
16, R_1 = R_3 = R_4 = R_5 = H, R_2 = Pren

Pren stands for $Me_2C = CH - CH_2$ -



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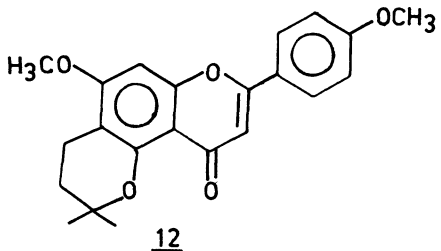

12

TABLE 3: NMR data[7]

COMPOUND or STRUCTURE	3-H[a]	8-H[a]	2',6'H[b]	3',5'-H[b]	4''H[c]	5''H[c]	$(CH_3)_2C$[a]	Ar-CH_2-	-CH=	-OCH_3[a]	-OH[a]	-$OCOCH_3$[a]
Natural Carpachromene	6.53	6.40	7.75	6.95	6.67	5.64	1.46				13.6 9.75	
Synthetic 1	6.27	6.58	7.23	6.75	6.40	5.65	1.40				9.75	
Diacetate of natural Carpachromene	6.54	6.80	7.84	7.24	6.51	5.77	1.48					2.32, 2.46(6H)
Diacetate of Pyranoflavone of P. Missionis	6.28	6.24	7.56	6.96	6.58	5.49	1.44					2.22, 2.32(6H)
Synthetic diacetate(17)	6.25	6.90	7.84	7.25	6.65	5.56	1.44					2.43(6H)
Dimethyl ether of natural carpachromene	6.55	6.70	7.79	6.99	6.75	5.72	1.46			3.87, 3.94(6H)		
Synthetic Dimethyl ether(2)	6.35	6.85	7.98	6.98	6.73	5.60	1.47			3.83, 3.84(6H)		
6	6.51		7.73	6.90			1.68,1.70 1.75(12H)	3.20,3.45 (2d,4H J=6.5Hz)	4.88- 5.19 (m,2H)	3.83(3H)		2.30, 2.40(6H)
10	6.55	6.80	7.75	6.97			1.37	3.30(d, 2H,J=7Hz)	5.12(t, 1H,J=7Hz)	3.87(3H)		2.38, 2.48(6H)
11	6.47	6.60	7.85	6.97			1.70, 1.80	3.37(d, 2H,J=8Hz)	5.23(t, 1H,J=8Hz)	3.85, 3.89(6H)		
13	6.42	6.57	7.62	6.97	6.75	5.65	1.50			3.90,S 3H	13.07	
16	6.25	6.62	7.80	6.92			1.65,1.70	3.0(d, 2H,J=8Hz)	5.05- 5.27(m, 1H)		10.25	

Unless stated otherwise (a) all signals are singlets; (b) all signals are doublets having J=9Hz, (c) all signals are doublets having J=10Hz.

The methyl ether (11) on acid cyclisation gave the corresponding chroman (12), m.p. 241-2°. Had it been 8-C-prenyl isomer, this cyclisation would not have occurred. Hence the second prenylation product is a 6-isomer (9).

Cyclodehydrogenation of 9 with DDQ gave the corresponding chromene (13), m.p. 189-90°; R_F 0.80 (solvent B); violet ferric reaction; NMR (see Table 3). It formed 5-methyl ether (2), m.p. 155-56°; R_F 0.5 (solvent B); its UV and NMR data (see Tables 1 and 3) were similar to chromene dimethyl ether (lit.[2] m.p. 156°).

In order to synthesise carpachromene itself, apigenin (3) was prenylated in the same manner as acacetin. It yielded a mixture of three compounds. The product obtained in maximum yield was identified at 7-O-prenyl-6,8-di-C,C-prenyl apigenin (14), m.p. 161-62°; R_F 0.9 (solvent A); bluish ferric reaction; it formed 6,8-di-C,C-prenyl apigenin (15) (see below) on heating with aq. morpholine.[8] The second product was characterised as 6,8-di-C,C-prenyl apigenin (15), m.p. 190-91°; R_F 0.8 (solvent A); brownish ferric reaction. It formed dimethyl ether (7) identical with the compound prepared from acacetin. The third nuclear prenylation product was established as 6-C-prenyl apigenin (16) m.p. 290-91°; R_F 0.55 (solvent A) by its NMR spectrum (see Table 3) and formation of dimethyl ether (11) identical with the compound prepared from acacetin.

6-C-Prenyl apigenin (16) when cyclodehydrogenated with DDQ afforded (1), m.p. 239-40° (lit.[2] m.p. 239-41°); dark violet ferric reaction; UV and NMR (see Tables 1 and 3). It formed diacetate (17); m.p. 240-41° (lit.[2] m.p. 240-41°); UV and NMR (see Tables 1 and 3). All these data agree with those described for carpachromene and its diacetate.

REFERENCES AND NOTES

1. Author to whom correspondence may be addressed.
2. K. Picker, E. Ritchie and W.C. Taylor, Aust. J. Chem., 29, 2003 (1976).
3. D.L. Dreyer and K.H. Park, Phytochem. 14, 1617 (1975).
4. All the compounds reported had the correct C, and H. analysis.
5. R_F values reported here refer to TLC carried out on silica gel G plates by using one of the following solvent systems: (A) toluene:ethyl formate: formic acid (5:4:1), (B) benzene:ethyl acetate (15:85), (C) benzene:ethyl acetate (1:4).
6. All UV spectra reported here were measured in methanol; the figures before parantheses represent λ_{max} values and within log ϵ values.
7. Unless stated otherwise, all the NMR spectra reported here were recorded on a 90MHz machine using $CDCl_3$ as solvent; and the chemical shifts have been expressed in δ values.
8. A.C. Jain, D.K. Tuli and A.K. Kohli, Synthetic Commun., under publication (1977).

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