DRAGON'S BLOOD FROM DRACAENA DRACO , STRUCTURE OF NOVEL HOMOISOFLAVANOIDS

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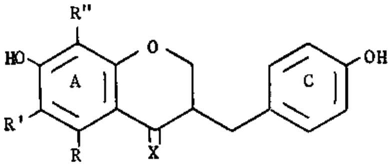
Abstract - Two novel homoisoflavans , 4',7-dihydroxy- (4) and 4',7-dihydroxy-8-methoxy- (5), were isolated from the resin "Dragon's blood", which is produced by Dracaena draco (Liliaceae) . In the same resin were also identified 4',7-dihydroxy- and 4',5,7-trihydroxy-6-methylhomoisoflavanones (1) and (3) , together with (2S)-4',7-dihydroxy-3'-methoxy-8-methylflavan (8) , (2S)-4',5-dihydroxy-7-methoxy-8-methylflavan (9) and 3,4'-dihydroxy-7-methoxyflavone (10) . Their structures were established on the basis of spectroscopic analysis and by synthesis .

As a part of our program of research on natural phenolic compounds we have investigated the constituents of the red resin "Dragon's blood" . This resin has been subject of investigation for several groups in the past years , particularly several new compounds have been isolated from Dragon's blood produced by the South - Asian Palma Daemonorops draco .
Diterpene acids[1] and several triterpenoids[2] were identified . Besides the well-known flavonoid pigments[3] dracorhodin and dracorubin , the corresponding compounds lacking the C-6 methyl group, nordracorhodin and nordracorubin were isolated[4] . Isolation of 5-methoxy-7-hydroxyflavan and 5-methoxy-6-methyl-7-hydroxyflavan was particularly interesting as they could be the precursors of the whole series of dimeric and trimeric flavonoids so far identified in the resin via various oxidative processes[5] .
In this paper we report the results of the examination of Dragon's blood produced by Dracaena draco (Liliaceae) , a tree which grows in the Canary Islands ; this resin was purified by means of medium pressure chromatography[6] and two groups of compounds were isolated : five homoisoflavonoids (1-5) and five flavonoids (6-10) , the yield of each being between 1 and 2% .
This resin has a completely different composition and therefore no connection , except for the folklore name , with the resin from Daemonorops .
The compounds (1-3) belong to the known class of homoisoflavan-4-ones and differ each other by variations in the oxygenation and methylation patterns of aromatic ring A ; however , (1) and (3) are novel natural products, only compound (2) has been already isolated from bulbs of Eucomis and Scilla sp.[7] The compounds (4) and (5) are two examples of the novel class of homoisoflavans , which have never been so far isolated as natural compounds .



(1) R = R'= R'' = H ; X = O
(2) R = OH ; R'= R'' = H ; X = O
(3) R = OH ; R'= Me ; R'' = H ; X = O
(4) R = R'= R'' = H ; $X = H_2$
(5) R = R'= H ; R'' = Me ; $X = H_2$

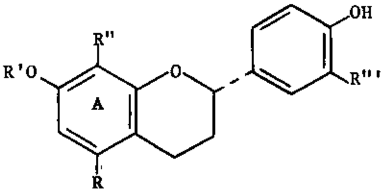
Compounds (1,3,4,5) were synthetized by condensing the corresponding chroman-4-ones with p-hydroxybenzaldehyde in acetic anhydride . Catalytic hydrogenation (by using 5% Pd on $BaSO_4$ or 10% Pd on charcoal as catalysts) of the resulting benzylidene derivatives , followed by their hydrolysis , gave (1) and (3) , or (4) and (5) , respectively . The IR and NMR spectra of the synthetic products were identical with those of the corresponding natural compounds , further confirm was given by direct chromatographic comparison (TLC) .

Table 1 . ^{1}H-NMR spectral data of natural homoisoflavonoids (1,3,4,5)[a]

	(1)	(3)	(4)	(5)
C-2	4.10 dd(12,7) 4.30 dd(12,4)	4.0-4.4 m	3.72 dd(10,8) 4.06 dd(10,3)	3.80 dd(10,8) 4.22 dd(10,3)
C-3	2.86 m	2.9 m	2.2-2.9 m	2.2 -2.8 m
C-4	-	-		
C-5	7.68 d(8)	12.50 s(OH)	6.80 d(8)	6.65 d(8)
C-6	6.52 dd(8,2)	2.95 s(Me)	6.30 dd(8,2)	6.47 d(8)
C-7	8.1 br s(OH)	8.2 br s(OH)	8.1 br s(OH)	-
C-8	6.34 d(2)	5.98 s	6.25 d(2)	3.79 s(OMe)
C-9	2.62 dd(12,8) 3.07 dd(12,4)	2.67 dd(12,8) 3.12 dd(12,4)	2.2 - 2.9 m	2.1 - 2.8 m

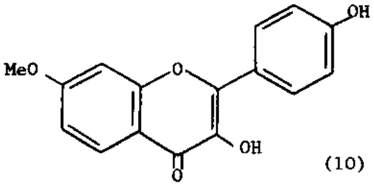
[a] The spectra were measured in acetone-d_6, except for the compound (5) which was measured in $CDCl_3$. Chemical shifts (δ) are given in ppm (from TMS as internal standard) . Coupling constants (J) are given in Hz . The following abbreviations are used : s = singlet ; d = doublet ; m = multiplet ; br = broad . Hydroxy signals of all the compounds were confirmed by the addition of D_2O . The chemical shifts and the coupling patterns of the signals of the A_2B_2 system of the ring C for all the compounds are not reported and they fit with the analog systems known in the literature . The assignments of the signals of the protons of the ring A were supported by decoupling measurements.

The second group of compounds isolated (6-9) belongs to the class of flavans . Their structures were established by analysis of the spectroscopic data .



(6) R = R' = R'''= H ; R'' = Me
(7) R = R' = R'' = H ; R'''= OMe
(8) R = R' = H ; R'' = Me ; R'''= OMe
(9) R = OH(OMe) ; R' = Me(H) ; R'' = Me; R'''= H

Spectroscopic data and optical rotation for (6) $[\alpha]_D^{20}$= +31.6° (c = 0.27 , MeOH) were in agreement with those of (2S)-4',7-dihydroxy-8-methylflavan isolated from bulbs of Narcissus pseudonarcissus[8] . The compound (7) , $[\alpha]_D^{20}$ = -6.89° (c = 0.58 , MeOH) is (2S)-4',7-dihydroxy-3'-methoxyflavan , already isolated as a racemate from the trunk wood of Iryanthera elliptica Ducke[9] .
The other two flavans (8) and (9) resulted to be (2S)-4',7-dihydroxy-3'-methoxy-8-methylflavan and 4',5-dihydroxy-7-methoxy-8-methylflavan respectively and are not known either as natural or as synthetic compounds .
Because of the poor quantity of (9) which was isolated , it was not possible to assign the exact substitution on ring A , therefore the two groups at C-7 and at C-5 could be interchanged .
The absolute configuration at C-2 of the four flavans was established as 2S on the basis of the correlation between the sign of the optical rotation with that of all the other natural flavans[4] .
Finally the analysis of the spectroscopic data of the compound (10) and of its diacetate (obtained by treatment with py/Ac_2O at r.t. for 3 h led to the structure of the new flavonol (10) .



(10)

Work is in progress in order to establish the absolute configuration at C-3 of the homoisoflavonoids (1-5) .

7-Hydroxy-3-(4-hydroxybenzyl)chroman-4-one (1) : white needles (from benzene) mp 194-195°C . UV ,λ_{max} (EtOH) 278 , 310 and 372 nm (ε 11600 , 7300 , 2600) . IR ,ν_{max}(nujol) : 3400 cm^{-1} (OH) ,1650 cm^{-1} (conj.CO) . Mass, m/e : M^{+}= 270.0903 ($C_{16}H_{14}O_4$ requires 270.0892) (100%) , 163 (53%) , 137(64%) , 107(76%) .

7-Acetoxy-3-(4-acetoxybenzyl)chroman-4-one (1a) : white needles (from ethanol) mp 111-112°C . $[\alpha]_D^{20}$ = -10.22° (c = 0.90 , $CHCl_3$) . IR , ν_{max}(nujol) : 1755 cm^{-1}(acetate CO) , 1670 cm^{-1}(conj.CO) . Mass , m/e : M^{+}= 354 . ^{1}H-NMR ($CDCl_3$) : δ 2.30 (6H, s , $COCH_3$) ; 2.6-3.4 (3H , m , $-CH-CH_2-Ph$) ; 4.25 (1H , dd , J = 12 and 7 Hz , $-CH_2-O-$) ; 4.47 (1H, dd , J = 12 and 4 Hz ,$-CH_2-O-$) ; 6.7-6.9 (2H, m , H-6 and H-8) ; 7.10 (2H, d , J = 0, H-3' , 5') ; 7.30 (2H, d , J = 0, H-2', 6') ; 8.0 (1H, d , J = 8 Hz , H-5) .

5,7-Dihydroxy-6-methyl-3-(4-hydroxybenzyl)chroman-4-one (3):mp 167-170°C . $[\alpha]_D^{20}$= -67.8° (c = 2.92 , MeOH) . λ_{max} (EtOH) 295 nm (ε 9700) . IR , ν_{max}(neat) : 3580 cm^{-1}(OH) . Mass, m/e : M^{+} = 300.1000 ($C_{17}H_{16}O_5$ requires 300.9980)(100%) , 193(47%) , 179(29%) , 166(65%) , 107(80%) .

7-Hydroxy-3-(4-hydroxybenzyl)chromane (4): mp 122-125°C . $[\alpha]_D^{20}$ = +54.1° (C = 1.09 , MeOH) . UV ,λ_{max} (EtOH) 281 nm (ε 4400) . IR ,ν_{max}(neat) : 3600 cm^{-1}(OH) . Mass , m/e : M^{+}= 256.1115 ($C_{16}H_{16}O_3$ requires 256.1099)(89%) , 149(56%) , 123(21%) , 107(100%) .

7-Hydroxy-8-methoxy-3-(4-hydroxybenzyl)chromane (5) : oil .$[\alpha]_D^{20}$= +36.93° (c = 1.58 , $CHCl_3$) . UV ,λ_{max} (EtOH)279 nm (ε 3500) . IR , ν_{max}(nujol) : 3400 cm^{-1}(OH) . Mass , m/e: M^{+}= 286.1215 ($C_{17}H_{18}O_4$ requires 286.1205)(100%) , 256(19%) , 179(26%) , 149(17%) , 107(94%) .

(2S)-4',7-Dihydroxy-3'-methoxy-8-methylflavan (8) : mp 60-64°C . $[\alpha]_D^{20}$ = -45.78° (c = 0.68 , MeOH) . UV ,λ_{max}(EtOH) 281 and 285 nm (ε 4200 , 3900) , UV + MeONa : bathochromic shift due to free 4'-hydroxyl group[10] . Mass, m/e : M^{+}= 286.1215 ($C_{17}H_{18}O_4$ requires 286.1205)(100%) , 272 (14%) , 256(17%) , 150(64%) , 137(79%) ; ^{1}H-NMR ($CDCl_3$) : δ 2.11 (3H, s , Me-8) ; 1.8-2.4 (2H, m , CH_2-3) ; 2.5-3.0 (2H, m , CH_2-Ph) ; 3.86 (3H, s , OMe) ; 4.96 (1H, dd , J = 9 and 3 Hz , H-2) ; 5.5 (1H, br s , OH) ; 6.34 (1H, d , J = 8 Hz , H-6) ; 6.76 (1H, d , J = 8 Hz , H-5) ; 6.8-7.0 (3H, m , H-2' , 5' , 6') .

(2S)-4',5-Dihydroxy-7-methoxy-8-methylflavan (9) : mp 151-154°C . $[\alpha]_D^{20}$= -9.40° (c = 0.489 , MeOH) . UV , λ_{max} (EtOH) 275 and 281 nm (ε 3200 , 2800) . Mass, m/e : M^{+}= 286.1215 ($C_{17}H_{18}O_4$ requires 286.1205)(30%) , 256(88%) , 150(40%) , 137(80%) , 120(100%) ; ^{1}H-NMR (acetone-d_6) : δ 2.05 (3H, s , Me-8) ; 1.7-2.3 (2H, m , CH_2-3) ; 2.5-2.8 (2H, m , CH_2-Ph) ; 3.67 (3H, s , OMe) ; 4.88 (1H, dd , J = 9 and 3 Hz , H-2) ; 6.08 (1H, s , H-6) ; 6.80 (2H, d , J = 0 , H-3' , 5') ; 7.25 (2H, d , J = 0 , H-2' , 6') ; 7.66 and 8.18 (2H, br s , OH) .

3,4'-Dihydroxy-7-methoxyflavone (10) : pale yellow solid , mp 219-220°C . UV,λ_{max}(EtOH) 352 nm (ε 22300) . IR , ν_{max}(KBr) : 3300 cm^{-1}(OH) , 1640 cm^{-1}(conj.CO) . Mass, m/e : M^{+}= 284(4%) ,270 (100%) , 255(29%) , 242(20%) , 199(50%), 164(71%) , 151(63%) . ^{1}H-NMR (acetone-d_6) : δ 3.90 (3H, s , OMe) ; 6.54 (1H, d ,J = 8 Hz , H-6) ; 6.56 (1H, s , H-8) ; 6.90 (2H, d , J = 0, H-3' , 5'); 7.54 (2H, d , J = 0, H-2' , 6') ; 7.60 (1H, d , J = 8 Hz, H-5) ; 8.9 (1H, br s , OH) .

Diacetate of (10) : ^{1}H-NMR ($CDCl_3$) : δ 2.28 and 2.30 (6H,s , $COCH_3$) ; 3.88 (3H, s , OMe) ; 6.7-6.9 (2H, m , H-6 and H-8) ; 7.12 (2H, d , J = 0 , H-3' , 5') ; 7.68 (2H, d , J = 0 , H-2' , 6'); 7.60 (1H, d , J = 8 Hz , H-5) .

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