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A GERANYL α-PYRONE FROM THE LEAF RESIN OF *DIPLACUS AURANTIACUS*

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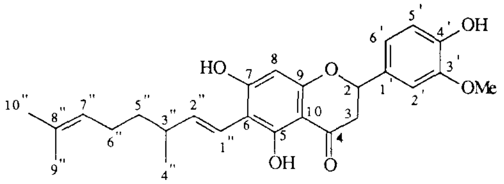
Key Word Index—*Diplacus aurantiacus*; Scrophulariaceae; leaf resin; novel geranyl α-pyrone; geranylflavanone.

Abstract—A novel prenylated α-pyrone has been isolated from the leaf resin of *Diplacus aurantiacus*. From its ^{1}H and ^{13}C NMR spectra, it is shown to be 3-(2-hydroxypropyl)-4-hydroxy-6-geranyl-2-pyrone. A geranylflavanone isolated from the same material is identified as 3′-methyl-6-geranyltaxifolin. The earlier tentative structure of 4′-methyldiplacol thus needs to be revised.

INTRODUCTION

Diplacus aurantiacus (Curtis) Jeps. (Scrophulariaceae) is a common shrubby plant native to coastal California. Its trivial name ‘sticky monkey flower’ refers to extremely rich production of leaf resin (up to 30% of leaf dry weight, [1]). This resin consists mostly of flavonoids with geranyl side chains. The flavanone 6-geranyleriodictyol (diplacone) and the dihydroflavonol 6-geranyltaxifolin (diplacol) were reported first [2]. Later their relevant 4′- (or 3′-?) methyl ethers were also found, along with 6-geranylnaringenin (mimulone) [1]. We obtained the leaf resin of some plants cultivated in the Botanical Garden at Darmstadt (under the synonym *Mimulus aurantiacus* Curt.) and analysed it in order to isolate the earlier reported geranyl flavonoids as markers. Diplacone, diplacol and mimulone were indeed isolated in good amounts, but we failed to find 4′-methyldiplacone and 4′-methyldiplacol. Instead, we isolated a product now identified as 3′-methyldiplacone. In addition we isolated a geranyl-substituted product with lower molecular weight, a prenyl α-pyrone and its structural identification is reported here.



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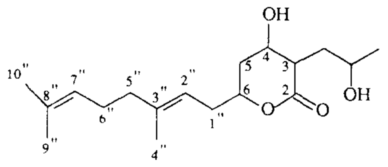

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RESULTS AND DISCUSSION

From the leaf resin of *Diplacus aurantiacus* we re-isolated the major flavonoids, diplacone (6-*C*-geranyleriodictyol), diplacol (6-*C*-geranyltaxifolin) and mimulone (6-*C*-geranylnaringenin). In addition [1, 2], we isolated an *O*-methyldiplacone **1** and a non-flavonoid geranyl-substituted product **2**.

Compound **1**, with $[M]^+$ 438 and the same MS fragmentation as the other geranyl derivatives, is a methylated geranyltaxifolin. Its UV spectrum is much the same as for the other compounds and does not indicate where the methyl group is placed. NMR spectral studies allow identification of its structure. The ^{13}C NMR spectra of **1**, diplacone, mimulone, and diplacol (Table 1) have many resonances in common. For instance the geranyl group and the A-ring signals for all four compounds are virtually identical, as are the C-ring signals of all but diplacol, the 3-OH analogue. These similarities are mirrored in the proton NMR spectra (Table 2). The differences between the substances lie mainly in the B-ring (and the C-ring in diplacol). The aromatic methoxy group of **1** can be located with certainty at C-3′ by comparing the B-ring carbon signals of diplacone with those of **1**. Because methylation causes a small, but significant downfield shift of the *para* carbon signal, examination of the C-6′ and C-1′ signals of **1** and diplacone allows the site of the methoxy group to be determined [3]. Comparison of the C-6′ and C-1′ signals of **1** and diplacone shows that the C-1′ signals are identical but the C-6′ signal of **1** is at lower field than that of diplacone, demonstrating conclusively that the

Table 1. ^{13}C NMR of *Diplacus aurantiacus* constituents*

C	1	Diplacone	Mimulone	Diplacol	2
2	78.7	78.4	78.4	83.0	165.0^a
3	42.2	42.2	42.1	71.7	101.1
4	196.5	196.4	196.5	198.0	164.7^a
5	160.6^a	160.6^a	160.6^a	160.4^a	101.0
6	107.6	107.5	107.5	107.7	161.1^a
7	164.3	164.3	164.3	164.5	
8	94.4	94.4	94.4	94.4	
9	160.5^a	160.5^a	160.5^a	160.1^a	
10	101.6	101.6	101.6	100.2	
1′	129.5	129.6	129.0	128.2	
2′	111.1	115.3	128.3	115.1	
3′	147.5	145.2	115.2	144.9	
4′	146.9	145.7	157.7	145.7	
5′	115.2	114.3	115.2	115.3	
6′	119.6	117.9	128.3	119.4	
1″	20.6	20.6	20.6	20.6	21.9
2″	122.4	122.4	122.4	122.4	121.8
3″	133.9	133.8	133.8	133.9	134.6
4″	15.9	15.9	15.9	15.9	16.1
5″	39.3	39.3	39.3	39.3	39.4
6″	26.2	26.2	26.2	26.2	26.3
7″	124.1	124.2	124.1	124.1	124.3
8″	130.7	130.7	130.7	130.7	130.8
9″	25.5	25.5	25.5	25.5	25.6
10″	17.6	17.6	17.6	17.6	17.7
3′-OMe	55.7				
$MeCHOHCH_2$					23.6
$MeCHOHCH_2$					64.2
$MeCHOHCH_2$					43.0

*Obtained in DMSO-d_6 at 50 MHz (flavanones) and 75 MHz (**2**).
^{a}Values in any column can be interchanged.

methoxy group is at C-3′. The original report [1] of the structure of the methyl ether of diplacone placed the methoxy group at C-4′ but raised the possibility that the 3′ isomer could not be ruled out. In fact the structure must now be revised to that of the 3′-methyl ether.

Although the UV spectrum of **2** mimics that of a flavanone, the carbonyl absorption frequency (1665 cm^{-1}) is too great for a 5-hydroxyflavanone [4]. The mass spectral fragmentation largely resembles that of the geranylflavanones and geranyldihydroflavonols, in which the dominant ions arise from the fragmentation of the side chain. Hence if the presence of geranyl substitution is assumed for this product, the remainder of the molecule must be smaller than a flavanone. This assumption is readily confirmed by the NMR data. The presence, in the leaf resin of *Diplacus aurantiacus*, of two products with geranyl side chains but lower molecular weight than the flavonoids, namely 332 and 306, had been mentioned earlier [1]. However, to our knowledge their structures have not yet been reported.

The ^{13}C NMR spectrum of **2** (Table 1) confirmed the presence of a geranyl group; the geranyl resonances were essentially identical to those of the four geranyl flavones and were in good agreement with reported spectra of geraniol [5, 6], if allowances are made for replacement of the terminal hydroxyl with an unsaturated carbon. Both IR and UV spectra were consistent with the presence of a pyrone ring, a hypothesis supported by the presence of three downfield signals from quaternary carbons. In fact published data for conrauanalactone [7], a 4-hydroxy-2-pyrone bearing an aliphatic side chain at C-6, support the α-pyrone structure if one takes into account that an additional aliphatic substituent is present. The ^{1}H NMR spectrum (Table 2) revealed two signals which disappeared upon addition of D_2O and are thus attributable to hydroxyl groups whose presence was also suggested by IR absorption in the 3100–3500 cm^{-1} region. A single aromatic proton signal was assigned to the lone pyrone ring hydrogen (H-5) for the following reasons: (i) spectra of model pyrones have shown that H-3 signals typically appear *ca* 0.8 ppm upfield from those of H-5 [Moreno-manas, M., personal communication]; [ii] typical C-4 and C-6 protons resonate at considerable lower field than the aromatic H observed for **2** [8]; (iii) addition of D_2O would exchange H-3 because of keto–enol tautomerism.

The nature of the side chain attached to C-3 was deduced from the NMR spectra as follows. The carbon spectrum had only three remaining unassigned signals, one CH, one CH_2, and one Me. The proton spectrum showed a methyl doublet signal which decoupling experiments showed to be coupled to a multiplet which was in turn coupled to a pair of double doublets. The fragment $MeCHCH_2$ was thus established; furthermore the chemical shift of the CH signal (H 4.14, C 64.2) indicates that an

Table 2. ^{1}H NMR of *Diplacus aurantiacus* constituents*

H	**1**	Diplacone	Mimulone	Diplacol	**2**
2	5.39 *dd*, $J = 2.8$, 13 Hz	5.34 *dd*, $J = 2.7$, 11.6 Hz	5.40 *dd*, $J = 2.8$, 12.2 Hz	5.67 *d*, $J = 7$ Hz	
3eq	2.68 *dd*, $J = 2.8$, 17 Hz	2.67 *dd*, $J = 3.2$, 17.3 Hz	2.68 *dd*, $J = 2.8$, 17.3 Hz		
3ax	3.30 *dd*, $J = 13$, 17 Hz	3,16 *dd*, $J = 12.5$, 17.2 Hz	3.24 *dd*, $J = 12.4$, 17.4 Hz	4.48 *dd* $J = 7$, 11 Hz	
8	5.98 *s*	5.96 *s*	5.96 *s*	5.94 *s*	
1″	3.12 *d*, $J = 7$ Hz	3.12 *d*, $J = 7.5$ Hz	3.11 *d*, $J = 6.8$ Hz	3.13 *d*, $J = 7$ Hz	3.14 *d*, $J = 8$ Hz
2″	5.13 *t*, $J = 7$ Hz	5.13 *t*, $J = 6.8$ Hz	5.13 *t*, $J = 7.2$ Hz	5.12 *t*, $J = 7$ Hz	5.24 *t*, $J = 8$ Hz
4″	1.70 *s*	1.70 *s*	1.70 *s*	1.70 *s*	1.72 *s*
7″	5.04 *t*, $J = 7$ Hz	5.04 *t*, $J = 6.8$ Hz	5.04 *t*, $J = 7.2$ Hz	5.04 *t*, $J = 7$ Hz	5.03 *t*, $J = 8$ Hz
9″[a]	1.60 *s*	1.60 *s*	1.60 *s*	1.60 *s*	1.64 *s*
10″[a]	1.53 *s*	1.53 *s*	1.53 *s*	1.53 *s*	1.56 *s*
2′	7.08 *d*, $J = 1.6$ Hz	6.74 *s*	7.31 *d*, $J = 8.6$ Hz	6.74 *s*	
3′			6.79 *d*, $J = 8.6$ Hz		
5′	6.79 *d*, $J = 8$ Hz	6.74 *s*	6.79 *d*, $J = 8.6$ Hz	6.74 *s*	
6′	6.90 *dd*, $J = 1.6$, 8 Hz	6.87 *s*	7.31 *d* $J = 8.6$ Hz	6.86 *s*	
5					6.08 *s*
5-OH	12.43 *s*	12.42 *s*	12.42 *s*	12.19 *s*	
MeCHOHCH$_2$					1.23 *d*, $J = 8$ Hz
MeCHOHCH$_2$					4.14 *m*
MeCHOHCH$_2$					2.56 *dd*, $J = 5$, 19 Hz
MeCHOHCH$_2$					2.46 *dd*, $J = 5$, 19 Hz

*Determined in DMSO-d_6 at 200 MHz (flavanones) and 300 MHz (**2**).

[a] Values for the 9 and 10 protons may be interchanged.

OH is attached. We propose 3-(2-hydroxypropyl)-4-hydroxy-6-geranyl-2-pyrone as the most likely structure for **2**, because most naturally occurring α-pyrones with long aliphatic side chains have them at C-6 [9]. An alternative structure in which the two side chains are interchanged cannot be ruled out. We tried to confirm the structure by an alkaline degradation, but it was not successful. No attempt to determine the configuration of the asymmetric carbon in the hydroxypropyl side chain was made. We believe **2** to be the first example of a natural α-pyrone with a geranyl side chain. It is assumed that **2** is identical with the earlier mentioned *Diplacus* product with $[M]^+$ at *m/z* 306 [1], so the second compound, $[M]^+$ at *m/z* 332, still needs to be elucidated.

EXPERIMENTAL

^{1}H NMR spectra and ^{13}C NMR spectra were recorded at 300 and at 75 Hz (**2**), or 200 and 50 MHz (flavanones) respectively. Mp: uncorr.

Diplacus aurantiacus was cultivated in the Botanical Garden at Darmstadt (kept under glass during the winter period). A voucher specimen is deposited in E. W.'s herbarium at Darmstadt. Freshly gathered aerial parts were briefly rinsed with Me_2CO to dissolve the leaf resin and the solution concd to yield a viscous dark brown residue. This material was subjected to CC on polyamide SC-6, eluted with toluene and increasing amounts of MeCOEt and MeOH. Non-polar fractions seemed to contain terpenoid-like substances which were not studied further. The flavonoids were partly separated by CC on silica (degradation, as mentioned [2], was not observed) and purified further by passage over polyamide and by crystallization from C_6H_6. We thus obtained diplacone, diplacol and mimulone, which were identified by their UV, NMR and mass spectra. These compounds were obtained as whitish powdery products by addition of C_6H_6 and/or petrol to highly concd solns in boiling Me_2CO or EtOH. They show the following melting points (not published previously): diplacone 170–173°, diplacol 150–153°, mimulone 120–122°. TheUV and mass spectral data of these products have been reported earlier [1, 2] and are therefore not repeated here, while the NMR spectra of the four flavanones and **2** are presented in Tables 1 and 2.

The methyldiplacone **1** exhibits mp 102–103°. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm 373 (sh), 294; $+AlCl_3$ 360 (sh), 300; $AlCl_3 + HCl$ 358, 309; +NaOH 333, 252; +NaOAc 331, 290 (sh); +NaOAc $+H_3BO_3$ 330 (sh), 295. MS *m/z* (rel. int.) 438 (73, $[M]^+$), 369 (13), 315 (77), 279 (11), 219 (100), 177 (18), 167 (20), 165 (56), 150 (21), 149 (31), 137 (18), 135 (19), 123 (14), 93 (15), 69 (38), 41 (10). NMR data see Table 1 and 2.

The pyrone (**2**) has mp 122–123°. UV λ_{max}^{MeOH} nm: 295; $+AlCl_3$ 362, 293, 230 (sh), unchanged with HCl; +NaOH 293; +NaOAc 289; +NaOAc + H_3BO_3 293. IR ν^{KBr} cm^{-1}: 3500–3100, 2960, 2920, 2720, 2670, 1665, 1575, 1430, 1410, 1270, 1130, 1070, 1000, 940, 825, and 755. MS (EI, *m/z*, rel. int.): 306 (40), 291 (2), 288 (1), 237 (31), 193 (21), 184 (46), 183 (54), 175 (27), 166 (32), 139 (100), 123 (96), 109 (29), 81 (35), 69 (96), 67 (56), 45 (93), 43 (90) and 41 (99). NMR data see Tables 1 and 2.

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