New Flavonoids from the Exudate of Baccharis bigelovii (Asteraceae)

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Z. Naturforsch. 41c, 946–948 (1986); received June 4, 1986

Baccharis bigelovii (Asteraceae), Leaf and Stem Exudate, Flavonoid Aglycones, 7-Benzoyl-chrysosin

Four flavonoids have been identified from the leaf and stem resin produced by Baccharis bigelovii (Asteraceae) in addition to twelve previously described aglycones. A flavonol (alnusin) and a dihydroflavonol (alnustinol) with 3,5,7-trihydroxy substitution had both been reported only twice before. The novel compound 2R,5,7-trihydroxy-flavanone is remarkable for its 2ß-substitution at the hetiocyclic ring. 7-Benzoyl-chrysosin is the first flavone aglycone found as ester and the first flavonoid aglycone at all that is esterified with an aromatic acid.

Introduction

In a recent publication we surveyed the known data on flavonoid aglycones in Baccharis species and reported the identification of a number of flavonoids from six species [1]. A dozen known flavonoids were reported from the leaf and stem resin of B. bigelovii A. Gray [1]. We now want to describe the structural elucidation of four additional compounds, two of which are novel natural products.

Material and Methods

Aerial parts of Baccharis bigelovii were collected in southern Arizona (26/12/84; Mule Mountains, Box Canyon Ranch, Cochise Co.; elev. 5600 ft). The plants form scattered muchbranched shrubs to 3 ft tall in rocky area on granitic substrate. A voucher is kept at the Herbarium of the University of Arizona in Tucson (ARIZ; G. Yatskievych 84-193). The air-dried material consisted mainly of stems, with few leaves. On rinsing with acetone, 333 g of plant material yielded 7.8 g of exudate as brown resin. The major flavonoid constituent, chrysosin, crystallized from this resin (ca. 200 mg). The residue was worked up by column chromatography, monitored by TLC, as described earlier [1]. Known flavonoids were identified by direct comparisons with authentic markers. Four additional products will be discussed now.

Compounds 1–4 were cited as 3–6 in ref. [1].

Results

The major flavonoid present in the resinous exudate of Baccharis bigelovii is the flavone chrysosin. (Compounds 1–4 were cited as 3–6 in ref. [1].)

Galangin and the new constituents 1, 2 and 3 were also obtained in crystalline form. These flavonoids are accompanied by apigenin, kaempferol, kae-7,4’-diMe, quercetin, isorhamnetin, pinocembrin, and pinobanksin. Luteolin and its 3′- and 4′-methyl
Table I. $^1$H NMR chemical shifts for compounds 1—4.

<table>
<thead>
<tr>
<th>Assignment</th>
<th>Compound 1*</th>
<th>Chrysin*</th>
<th>Compound 2+</th>
<th>Acetate 2a+</th>
<th>Compound 3§</th>
<th>Compound 4*</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-2ß</td>
<td>–</td>
<td>–</td>
<td>4.56 d (12)</td>
<td>5.40 d (12)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>H-3a</td>
<td>6.76 s</td>
<td>6.80 s</td>
<td>5.08 d (12)</td>
<td>5.73 d (12)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>H-3ß</td>
<td>6.71 d (2)</td>
<td>6.28 d (2)</td>
<td>–</td>
<td>–</td>
<td>2.88 dd (15.5, 2)</td>
<td>–</td>
</tr>
<tr>
<td>H-5</td>
<td>7.00 d (2)</td>
<td>6.68 d (2)</td>
<td>6.14 s</td>
<td>6.75 s</td>
<td>5.97 d (2)</td>
<td>–</td>
</tr>
<tr>
<td>H-6</td>
<td>7.91 dd (8, 1.5)</td>
<td>8.12—8.05 m</td>
<td>7.58—7.43 m</td>
<td>7.48—7.41 m</td>
<td>7.71 dd (8, 1.5)</td>
<td>8.21 dd (8, 2)</td>
</tr>
<tr>
<td>H-7/H-6'</td>
<td>7.65—7.48 m</td>
<td>7.65—7.59 m</td>
<td>7.48—7.38 m</td>
<td>7.62—7.48 m</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5-OH</td>
<td>12.79 s</td>
<td>12.90 s</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>OCH$_3$</td>
<td>3.96 s</td>
<td>3.79 s</td>
<td>2.43 s, 2.36 s, 6.63 bs</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Others</td>
<td>7.68 dt (8, 1)</td>
<td></td>
<td>(3-OH)</td>
<td>1.99 s</td>
<td>9.63 s, 6.54 d (2)</td>
<td>6.61 bs</td>
</tr>
<tr>
<td></td>
<td>7.65—7.48 m (2H)</td>
<td></td>
<td>(3 × OAc)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* In CDCl$_3$, § in (CD$_3$)$_2$CO, in DMSO-d$_6$ (J in Hz, δ in ppm).

ethers (chrysoeriol and diosmetin) were observed as trace constituents.

**Structure elucidation of compounds 1—4**

The $^1$H NMR spectrum of compound 1 shows only aromatic protons (see Table I). The singlet at δ 6.76 ppm is assignable to H-3, while the two one-proton doublets at δ 6.71 and 7.00 are assigned to H-6 and H-8, respectively, in a 5,7-di-oxygenated flavone. The presence of two different monosubstituted benzene rings is shown by the multiplets between δ 7.48 and 8.12. The signal in the far-down field (δ 12.79) shows the presence of a hydroxy group which is hydrogen-bonded to the carbonyl group (OH at C-5). Thus, the substituent must be located at C-7. The identification of this substituent as benzoate has been made through the NMR multiplets at δ 8.21, 7.68 and 7.65—7.48, which agree closely for H-2/H-6, H-4 and H-3/H-5, respectively, in a benzoic aromatic ester comparing with calculated values [3]. The mass spectrum supports the proposed structure by the molecular peak at m/z 358 and two unusually strong ions at m/z 105 (PhCO) and 77 (Ph), arising from the B-ring fragment as well as from the benzoic ester. Alkaline hydrolysis of 1 (KOH 8.5%, room temp., overnight) yields the flavone chrysin and benzoic acid. Both compounds are identified by their spectroscopic data and by comparisons with authentic markers. Hence the structure of 1 is undoubtedly 7-benzoyl-chrysin.

The $^1$H NMR spectrum of compound 2 shows two one-proton doublets at δ 4.56 and 5.08 ppm, that suggest the structure of a dihydroflavonol. Like compound 1 it has an unsubstituted B-ring (multiplet between δ 7.58 and 7.43) and a OH-group at C-5 (singlet at δ 11.36), but a methoxy group (singlet at δ 3.96) and only one proton at the A-ring (singlet at δ 6.14). Acetylation of 2 affords the triacetate 2a and confirms the dihydroflavonol structure by shifting the H-2/H-3 signals at low field and by the existence of an aliphatic acetyl (singlet at δ 1.99). In total the spectroscopic data lead us to establish the structure of compound 2 as 3,5,7-trihydroxy-6-methoxyflavanone.

Compound 3 has a molecular formula of C$_{15}$H$_{12}$O$_5$, M$^+$ 272. Its chromatographic behaviour and its UV-spectrum point to a flavanone having three hydroxy groups. The singlets at δ 12.04 and δ 9.63 ppm for OH at C-5 and at C-7 as well as two doublets at about δ 6 ppm for H-6 and H-8 are easily assigned. Once again, the NMR signals indicate an unsubstituted B-ring (multiplets at δ 7.71, 2H, and at 7.42, 3H), which is confirmed by strong ions at m/z 105 and 77 in the mass spectrum. Thus, the remaining signals and the third hydroxy group must be those corresponding to the heterocyclic ring. The β-axial configuration of the OH at C-2 can be deduced from the coupling constant (2 Hz) observed between such hydroxyl (δ 6.54, d) and the transaxial H-3α (δ 3.21, dd). Compound 3 is described as 2ß,5,7-trihydroxyflavanone.

Compound 4, M$^+$ 300, molecular formula C$_{16}$H$_{12}$O$_6$, also has an unsubstituted B-ring (δ 8.21 ppm, 2H, and 7.55, 3H). Further, an aromatic proton (δ 6.63, s) and a methoxy group (δ 4.06, s) can be deduced from the NMR spectrum. It is assumed to
be either 6-methoxy- or 8-methoxy-galangin. Differentiation between 6- and 8-methoxy isomers is possible by the relative intensities of the peaks corresponding to \( M^+ \) and \( M^- - 15 \) [4]. In this case, \( M^- - 15 < M^+ \) indicates 6-methoxy substitution. The spectroscopic properties of compound 4 are in fact identical with those reported for 3,5,7-trihydroxy-6-methoxy-flavone [5]. Direct comparison with a sample of synthetic alnusin confirms the identity.

![Diagram](image)

It is obvious that flavonoids with unsubstituted B-ring are predominant in the leaf and stem resin of *Baccharis bigelovii*. Compounds 1–4 are either rare or novel natural products. 3,5,7-Trihydroxy-6-methoxy-flavanone (2) was reported for the first time from male flowers of *Alnus sieboldiana* (Betulaceae) and was named alnustinol [6]. We assume that it there also occurs as a constituent of the resinous material, similar to the well known existence of terpenoids [7] and flavonoid aglycones [8] in bud exudates of Betulaceae. It was found a second time in roots of *Chromolaena chasleae* (Compositae) [9]. Alnustinol is still the only known dihydroflavonol with this pattern of O-substitution. 3,5,7-Trihydroxy-6-methoxy-flavone [4] which exhibits the same substitution pattern, was first reported from catkins of *Alnus sieboldiana* and named alnusin [6]. The flavonol was found in roots of *Chromolaena chasleae* as well [9].

Compounds 1 and 3 are both novel products with unusual substitution. 7-Benzoyl-chrysin (1) is the first flavone aglycone to be found as a natural ester, and it is the only flavonoid aglycone known that has an aromatic acid as acyl moiety (cf. [10]). 2β,5,7-Trihydroxylflavanone (3) was reported previously as a synthetic product [11], while its 7-methyl ether was found as constituent of the bud exudate of poplars (*Populus* spp., cf. [12]).

Acknowledgements

The authors want to thank George Yatskievych (Dpt. of Biology, Indiana University, Bloomington, Ind., USA) for collecting the plant material, Prof. Dr. J. Chopin (Laboratoire de Chimie Biologique, Université Claude Bernard Lyon I, France) for providing a sample of synthetic alnusin, and Mrs. K. Mann (Darmstadt) for skillful technical assistance. E. W. gratefully acknowledges financial support by the Deutsche Forschungsgemeinschaft.