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BISABOLANE SESQUITERPENES AND A 2-PHENOXYCHROMONE FROM *ROSA WOODSII* LEAVES

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Key Word Index—*Rosa woodsii*; Rosaceae; bisabolane sesquiterpene; 2-phenoxychromone; chemotaxonomic index of genus *Rosa*.

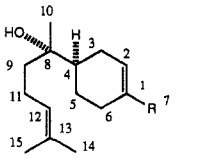
Abstract—Two novel bisabolanoids, hamanasal A [=4*R*:8*S*-8-hydroxybisabola-1(2),12(13)-dien-7-al] and hamanasol A [=4*R*:8*S*-7,8-dihydroxybisabola-1(2),12(13)-diene] were isolated from leaves of *Rosa woodsii*. The absolute configuration at C-4 of these compounds, which agreed with that of bisaborosaol A from *R. rugosa* leaves, was a common feature of the bisabolanoids from the genus *Rosa*. *R. woodsii* also contained a 2-phenoxychromone derivative which has been isolated as a rare flavone derivative of *R. rugosa*.

INTRODUCTION

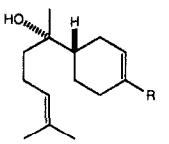
Monoterpenes of *Rosa* species are well studied [1], because of their commercial demands. By contrast, sesquiterpenes of *Rosa* species are quite rare, and probably the essential oils of *R. damasceana* [2] and *R. chenensis* [3] are the only examples. Recently, we found that *R. rugosa* leaves are rich in several sesquiterpenoids, consisting of carotanoids [4–6], bisabolanoids [7] and acoranoids [6], all of which were obtained from glandular trichomes [8]. In other wild roses, such glandular trichomes or other secretory organs are rare, except in *R. rugosa* varieties (e.g. *R. rugosa* var. *plena*) and hybrid *rugosa*. Indeed, any carotane aldehyde has, so far, not been detected in wild roses which do not possess glandular trichomes on the leaves. However, during the investigation of methanolic leaf extracts from *R. woodsii*, some compounds showing α sesquiterpene-like nature were detected.

RESULTS AND DISCUSSION

Silica gel column chromatography combined with TLC dinitrophenylhydrazine reagent [9] monitoring showed the presence of a sesquiterpene aldehyde. The purified compound showed in the ^{1}H NMR spectrum a formyl proton at δ_H9.44 together with two olefinic protons (δ_H6.85, *br m*, and 5.14, *t*, respectively). In addition, the presence of two allylic methyl signals (δ_H1.70 and 1.63) and a singlet methyl (δ_H1.18) signal indicated a C-7-oxo-bisabolane derivative. The ^{13}C NMR spectra showed the presence of a tertiary hydroxylated (δ_C74.1) and an aliphatic methine (δ_C 43.1) carbon, revealing the presence of 7-oxo-8-hydroxybisabola-1(2),12(13)-diene (**1**, hamanasal A). When bisaborosaol A [**3**, (4*R*:8*S*)-7-methoxycarbonyl-8-hydroxybisabola-1(2),12(13)-diene] was treated with lithium aluminium hydride and then with manganese dioxide, (4*R*:8*S*)-7-oxo-8-hydroxybisabola-1(2),12(13)-diene was obtained. The spectroscopic data, including optical rotation [7], of this compound were identical to those of **1**. Compound **1** was dextrorotatory ($[\alpha]_D^{23}+71°$) and was assigned *R* configuration at C-4. Although (4*S*)-7-oxo-8-hydroxybisabola-1(2),12(13)-diene has been isolated from some Compositae plants [10, 11]



	R	
1	CHO	hamanasal A
2	CH_2OH	hamanasol A
2a	CH_2OAc	
3	CO_2Me	bisaborosaol A
4	CO_2H	hamanasic acid A



Bisabolane derivative of Compositae origin

R=Me, CH_2OH, CHO, CO_2Me

as a naturally occurring compound, **1** with 4*R* was a novel natural compound. *R. woodsii* was thus found to be a source plant of 4*R*-bisabolanoid, as *R. rugosa* [7]. This 4*R* configuration, the inverse to bisabolanoids of Compositae plants [10–14], was a characteristic feature of bisabolane sesquiterpenes from the genus *Rosa*.

In addition to compound **1**, the corresponding alcohol (**2**) was present in a polar fraction. Crude **2** obtained from *R. woodsii* showed some signals attributable to an 8-hydroxybisabolene derivative, and signals at δ_H4.01 (2H, *br s*) were assigned to a C-7 hydroxymethyl group. The ^{1}H NMR spectrum of 7,8-dihydroxybisabola-1(2),12(13)-diene derived from **3** [7] agreed well with that of **2**. The monoacetate **2a** from **2** was also dextrorotatory, as the monoacetate derived from **3** whose C-4 absolute configuration was proved to be *R* [7] as well as other bisabolanoids of *Rosa* origin. Because the ^{13}C NMR spectra of **2a** from different origins were in good accord, compound **2** should possess the same 4*R*:8*S* configuration as **1**. From a Compositae plant, Matos *et al.* have isolated (4*S*)-7-hydroxy-α-bisabolol [=(4*S*:8*S*)-7,8-dihydroxybisabola-1(2),12(13)-diene] whose monoacetate was laevorotatory [12]. Compound **2** having the 4*R* configuration is also reported for the first time from natural sources. Compound **2** is probably the precursor of **1**.

Although the C-7 carboxylic acid (hamanasic acid A, **4**) and its C-7 methoxycarbonyl derivative (bisaborosaol A, **3**) have been found in leaves of *R. rugosa* in high concentration, the C-7 carbaldehyde and carbinol (**1** and **2**, respectively) have not been found in this plant so far, in spite of our careful investigation. By contrast, *R. woodsii*

did not contain **3**, while only a trace amount of **4** was detected on TLC. However, identification of **4** by ^{1}H NMR failed. These facts may indicate that the oxygenation and modification levels of bisabolane sesquiterpenes is clearly different between *R. woodsii* and *R. rugosa*. Such a clear difference in the oxygenation level may suggest strict regulation of oxygenation at C-7 in these plants. *R. woodsii* is expected to lack an oxidase catalysing oxygenation of the C-7 formyl carbon to carboxylic carbon. This difference in the sesquiterpene metabolism seems to have evolved as the genus *Rosa* emerged.

During the isolation of **1**, no carotane sesquiterpenes have been found so far. However, 6-demethoxy-4′-*O*-methylcapillarisin, a 2-phenoxychromone derivative previously isolated from *R. rugosa* as a rare flavonoid [15], was found in *R. woodsii* as a major flavonoid. The presence of the 2-phenoxychromone derivative in *R. woodsii* revealed a close taxonomic relationship between this plant and *R. rugosa*, because 2-phenoxychromones are rare compounds as secondary metabolites of higher plants [15] and are thus a clear chemotaxonomic index. On the other hand, some commercial roses (*R. hybrida*, e.g. Peace) do not contain the 2-phenoxychromone even in a trace amount.

EXPERIMENTAL

The plant materials (1.3 kg fresh leaves) were collected in a suburban area of Edmonton, Alberta, Canada in mid-August. The leaves were immediately soaked in 90% MeOH for 3 weeks. The MeOH was removed from the methanolic extracts to give a water suspension (600 ml), which was partitioned against 1400 ml benzene to yield 14.8 g of tar-like benzene-soluble material. The extracts were chromatographed in a silica gel column (180 g) and 13 frs (each 200 ml) were obtained as follows: fr. A-1–5; eluted with 23% EtOAc–*n*-hexane, fr. A-6–13; 50% EtOAc–*n*-hexane. Frs A-7–12 (2.0 g) were combined and further chromatographed in a silica gel column (90 g). Following a wash with 1–4% MeOH–$CHCl_3$ (fr. B-0), eluates of 10% MeOH–$CHCl_3$ (50 ml × 4) were obtained (fr. B-1–4). Fr. B-2 (320 mg) containing **1** was re-column chromatographed in a silica gel column (50 g) eluted with 10% EtOAc–benzene (fr. C-1–75, each 12 ml). Compound **1** eluted in fr. C-41–50 was purified by prep. TLC (benzene–EtOAc 17:3 and *n*-hexane–EtOAc–HCO_2H 250:25:1) and HPLC (Inertsil PREP-SIL, 25% isoPrOH–*n*-hexane, UV 230 nm), to give 17 mg of compound **1**. During the third CC, 6-demethoxy-4′-*O*-methylcapillarisin was also obtained, and the pure compound (12 mg) was isolated by prep. TLC (*n*-hexane–EtOAc–HCO_2H, 150:75:1). The combined fr. B-12 and B-13 (420 mg) was chromatographed in a silica gel column (60 g) eluted with 25% EtOAc–benzene (800 ml) and then EtOAc alone (500 ml). Compound **2** eluted in the EtOAc–benzene (700–800 ml) and EtOAc (500 ml) frs were isolated by prep. TLC (benzene–EtOAc 1:1 and $CHCl_3$–MeOH 25:1) to give 11 mg of a syrup of crude **2**. Acetylation (Ac_2O–pyridine) gave the monoacetate **2a** (6 mg). The novel bisabolane sesquiterpenes **1** and **2** were named hamanasal A and hamanasol A, respectively.

(4R:8S)-7-*Oxo*-8-*hydroxybisabola*-1(2),12(13)-*diene* (*hamanasal A*, **1**). Syrup. $[\alpha]_D^{23}$ +71° (MeOH; *c* 0.5). FIMS *m/z* (rel. int.): 237 $[M+1]^+$ (41), 236 $[M]^+$ (100), 219 (23). EIMS *m/z* (rel. int.): 218 $[M-H_2O]^+$ (7.6), 203 (2.7), 189 (3.7), 175 (13), 162 (6.8), 148 (6.9), 135 (11), 133 (14), 121 (13), 119 (12), 109 (73), 107 (22), 105 (22), 93 (45), 91 (34), 81 (23), 79 (31), 77 (20), 69 (100), 67 (34), 55 (46), 43 (40), 41 (92); ^{1}H NMR (500 MHz, $CDCl_3$): δ9.44 (*s*, H-7), 6.85 (*ddd*, *J* = 3, 2 and 2 Hz, H-2), 5.14 (*br t*, *J* = 7 Hz, H-12), 2.52 (*br d*, *J* = 20 Hz, Ha-6), 2.51 (*m*, Ha-3), 2.24 (*m*, Hb-6), 2.07 (*m*, H_2-11), 2.03 (*m*, Hb-3), 1.94 (*m*, Ha-5), 1.70 (*s*, H_3-14), 1.69 (*m*, H-4), 1.63 (*s*, H_3-15), 1.56 (*t*, *J* = 7 Hz, H_2-9), 1.22 (*dddd*, *J* = 13, 12, 12 and 5 Hz, Hb-5), 1.18 (*s*, H_3-10); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT and CH-COSY): δ193.9 (CH-7), 151.3 (CH-2), 141.3 (C-1), 132.2 (C-13), 124.2 (CH-12), 74.1 (C-8), 43.1 (CH-4), 39.6 (CH_2-9), 27.5 (CH_2-6), 25.7 (Me-14), 23.8 (Me-10), 22.7 (CH_2-5), 22.3 (CH_2-11), 22.2 (CH_2-3), 17.7 (Me-15). All the properties agreed with those of **1** synthesized from bisaborosaol A (**3**). The ^{13}C NMR signals [7] were re-assigned by DEPT and CH-COSY.

(4R:8S)-7,8-*Dihydroxybisabola*-1(2),12(13)-*diene* (*hamanasol A*, **2**). Syrup. ^{1}H NMR (270 MHz, $CDCl_3$): δ5.70 (*br m*, H-2), 5.14 (*br t*, *J* = 7 Hz, H-11), 4.01 (*br s*, H_2-7), 1.69 (*s*, H_3-14), 1.63 (*s*, H_3-15), 1.53 (*t*, *J* = 8 Hz, H_2-9), 1.15 (*s*, H_3-10). 3.1 mg of **2** further purified by TLC (*n*-hexane–EtOAc–HCO_2H, 25:25:1) was acetylated (Ac_2O–pyridine) and 2.0 mg of **2a** was obtained (55% yield).

7-O-*Acetyl derivative of* **2** (**2a**). Syrup, total 6 mg. $[\alpha]_D^{23}$ +52° (EtOH; *c* 0.09). FIMS *m/z* (rel. int.): 280 $[M]^+$ (100); ^{1}H NMR (270 MHz, $CDCl_3$): δ5.77 (*br m*, H-2), 5.13 (*br t*, *J* = 7 Hz, H-11), 4.46 (*br s*, H_2-7), 2.07 (*s*, OAc-7), 1.69 (*s*, H_3-14), 1.63 (*s*, H_3-15), 1.52 (*t*, *J* = 8 Hz, H_2-9), 1.15 (*s*, H_3-10); ^{13}C NMR (68 MHz, $CDCl_3$, CH-COSY): δ170.6 (OCOMe-7), 132.2 (C-13), 131.4 (C-1), 125.7 (CH-2), 123.9 (CH-12), 73.8 (C-8), 68.0 (CH_2-7), 42.6 (CH-4), 38.8 (CH_2-9), 26.4 (CH_2-3), 25.4 (CH_2-6), 25.2 (Me-14), 23.5 (Me-10), 23.0 (CH_2-5), 21.8 (CH_2-11), 20.5 (OCOMe-7), 17.2 (Me-15). All the proton and carbon signals of **2a** agreed with those of **2a** synthesized from bisaborosaol A (**3**).

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