VARIATIONS IN THE CHEMICAL SHIFT OF THE 5-HYDROXYL PROTON OF 7-*O*-PRENYLATED FLAVANONES[1]

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Abstract —— In ^{1}H nmr examination of 6- or 8-prenylated flavanone 7-methyl and 7-prenyl ethers, the signals of hydrogen-bonded hydroxyl proton appeared in relatively narrow region. Relatively large solvent effect was observed on the signal of 6-prenylflavanone 7-methyl and 7-prenyl ethers.

In the previous ^{1}H nmr studies on flavonoids having a 3-methyl-2-butenyl group (prenylflavonoids),[2] we reported that the signal of hydrogen-bonded hydroxyl proton (5-OH) of 6-prenylflavonoids appears further downfield (0.25 – 0.30 ppm, measured in acetone-d_6) than that of 6-unsubstituted flavonoids having the same B and C rings. In contrast, the OH signal of 8-prenylflavonoid appears further upfield (0.04 – 0.10 ppm) than that of flavonoids having the same B and C rings and no side chain. The observation of the C-prenylation effects on the 5-OH signals is useful method especially for the characterization of 6- and 8-prenylated flavanones, because the measurement requires only a small amount of sample (less than 200 μg in routine measurement). The other unambiguous method of the structure determination of these prenylflavanones is an observation of spin-spin coupling between 5-OH and C-6 by ^{13}C nmr measurement (nondecoupling, HMBC spectra, *etc.*),[3] but this method needs relatively large amount of sample compared with our ^{1}H nmr method.

Previously, we pointed out that the chemical shift of 5-OH signal of 8-*C*,7-*O*-diprenylpinocembrin obtained from *Helichrysum rugulosum*[4] is not compatible with a rule of the *C*-prenylation effect on the signal.[5] Therefore, we described that the structure of the compound would be revised to 6-*C*,7-*O*-diprenyl-pinocembrin. Recently, we reported the following prenylation effect on 7-*O*-methylisoflavones:[6] the 5-OH signal of 8-prenylated 7-*O*-methylisoflavone appears further downfield (0.08 ppm) than that of 7-*O*-methyl-isoflavone having no side chain as well as that of 6-prenylated 7-O-methylisoflavone (0.21 ppm), that is, the signals of prenylisoflavone 7-methyl ethers appear in relatively narrow region (δ 13.04 – 13.17). The chemical shift of the 5-OH signal changes in dependence on the frequency of the observational spectrometer.[6] Thus, comparison of the 5-OH signal of 7-*O*-methylisoflavones needs measurement under same conditions (frequency of instrument and solvent). The above findings indicated that we need more

detail nmr examination of 7-*O*-prenylated flavanones. In this paper, we discuss the *C*-prenylation effect on the 5-OH signal of 7-*O*-prenylpinocembrin (**7**)[7] and pinostrobin (**10**).[8] The evaluative samples (**2** – **7**) were obtained by prenylation of pinocembrin (**1**)[9] with 1-bromo-3-methyl-2-butene.[10] The structures of C-prenylated flavanones (**2**,[11] **3**,[12] **5**, and **6**) were elucidated with the ^{13}C nmr method, respectively.[13]

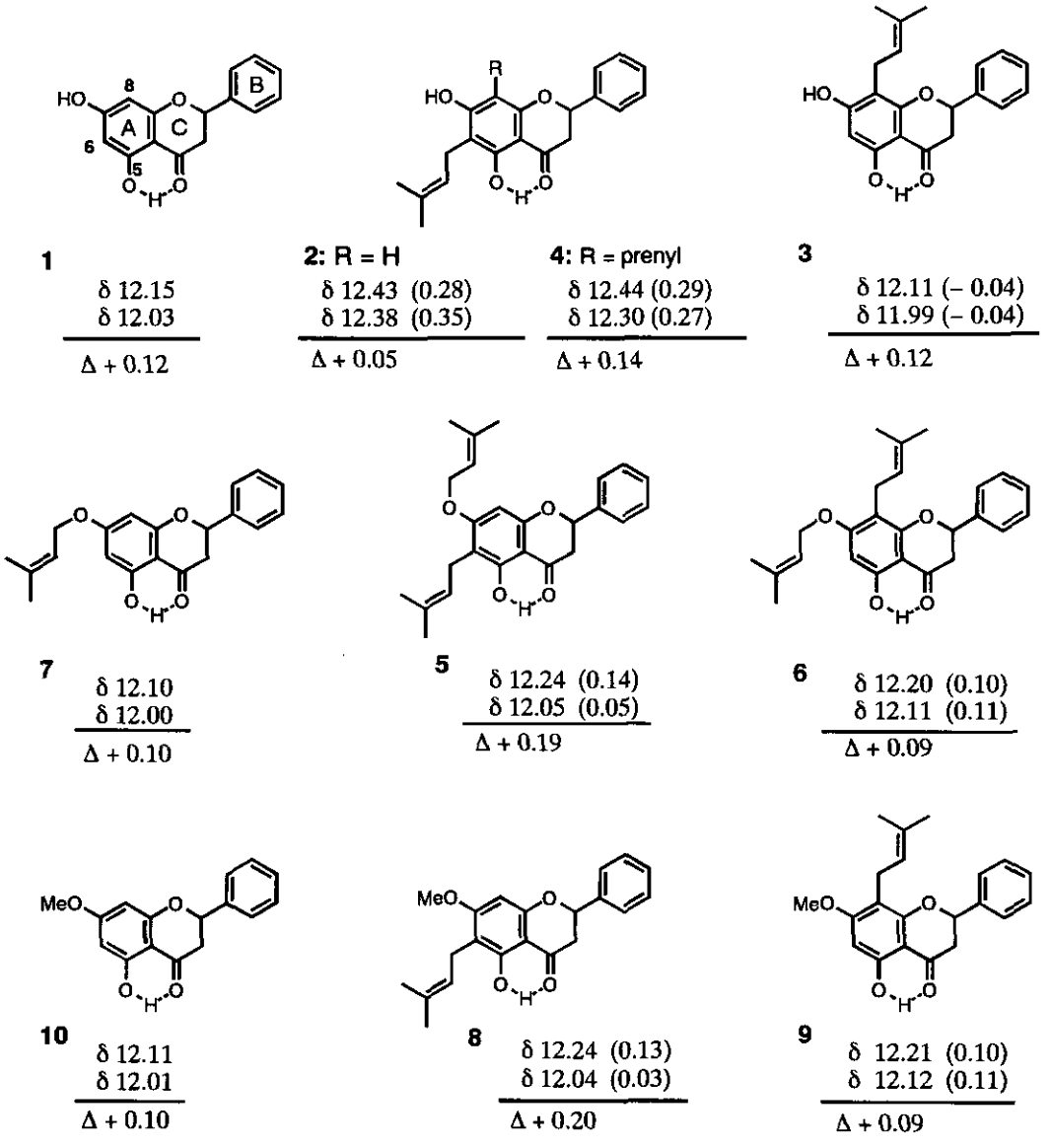

Figure 1 Chemical shifts of the 5-OH signal of pinocembrin derivatives

(The chemical shifts shown in the upper lines were measured in acetone-d_6, and in the middle lines were measured in $CDCl_3$ with 400 MHz instrument. Δ is difference of the chemical shifts [δ (in acetone-d_6) – δ (in $CDCl_3$)]. The difference of the chemical shifts between *C*-prenylated flavanone and corresponding non-prenylated compound was shown in the parenthesis.)

The chemical shifts of the 5-OH signal of these compounds (**1** – **7**), 6-, 8-, and non-prenylated pinostrobin (**8**,[11] **9**,[14] and **10**)[15] are shown in Figure 1 (measured in $CDCl_3$ and acetone-d_6 with 400 MHz instrument).

The 5-OH signal of 8-prenylpinostrobin (**9**) appeared further downfield (0.10 ppm, in acetone-d_6) than that of pinostrobin (**10**) as well as that of 6-prenylpinostrobin (**8**, 0.13 ppm). The signal of 8-*C*,7-*O*-diprenylpinocembrin (**6**) was also observed further downfield (0.10 ppm, in acetone-d_6) than that of 7-*O*-prenylpinocembrin (**7**) as well as that of 6-*C*,7-*O*-diprenylpinocembrin (**5**, 0.14 ppm).

The 5-OH signal of all 6-prenylated flavonoids appears further downfield than that of their 8-prenylated isomers when measured in acetone-d_6.[2] On the other hand, when the ^1H nmr spectra were measured in $CDCl_3$, the signal of the 6-prenylated 7-*O*-methylflavanone (**8**) and 7-*O*-prenylflavanone (**5**) showed upfield shift (0.06 – 0.08 ppm) compared with that of their 8-prenylated isomers (**6** and **9**). Previously, we described that the structure of diprenylpinocembrin obtained from *Helichrysum rugulosum* would be revised by their chemical shift of 5-OH signal.[5] Although, the data obtained here suggested that the structure determination with the chemical shift of 5-OH is unsuitable for the flavanone.

The following relatively large solvent effect was found on the signals of **5** and **8**. The chemical shift of the 5-OH signal changes in dependence of measurement solvent as shown in Figure 1. When the spectra of 7-hydroxyflavanones (**1**, **2**, **3**, and **4**) were measure in acetone-d_6, the signals appeared further downfield (0.05 – 0.14 ppm) than observed in $CDCl_3$ (Figure 1). The signals of **6**, **7**, **9**, and **10** in acetone-d_6 also showed downfield shift (0.09 – 0.10 ppm) compared with the same signals that were observed in $CDCl_3$. On the other hand, the signals of 6-prenylated 7-*O*-methylflavanone (**8**) and 7-*O*-prenylflavanone (**5**) in acetone-d_6 appeared further downfield (0.20 and 0.19) than observed in $CDCl_3$, respectively.[16] The solvent effect may be useful for the characterization of these flavanones.

It is noteworthy that the chemical shifts of the 5-OH signal of both 6-*C*,7-*O*-diprenylpinocembrin (**5**, δ 12.05 in $CDCl_3$ with 400 MHz) and 8-*C*,7-*O*-diprenylpinocembrin (**6**, δ 12.11) differed from that of natural 8-*C*,7-*O*-diprenylpinocembrin (δ 12.30 in $CDCl_3$) reported by Bohlmann and Misra.[4,17] The above data suggested that the structure of the diprenylflavanone obtained from *Helichrysum rugulosum* is still not completely elucidated because the structure was proposed without unambiguous method.

REFERENCES AND NOTES

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10. A mixture of **1** (500 mg, 2 mmol), 1-bromo-3-methyl-2-butene (0.4 ml, 2.7 mmol), KOH (300 mg, 5.4 mmol), 18-crown-6 (85 mg) in methanol (30 ml) was allowed to stand at room temperature for 28 h. The reaction mixture was treated as usual, and isolated by silica gel column chromatography and preparative tlc to give **2** (51 mg, 8%), **3** (81 mg, 13%), **4**[4] (8 mg, 1%), **5** (21 mg, 3%), **6** (5 mg, 1%), **7** (19 mg, 3%) and the starting material (210 mg, 42%).
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13. **2**; δ_C (acetone-d_6) 95.5 (d, ^1J = 162 Hz, C-8), 109.4 (br s, C-6), **3**; δ_C 96.7 (dd, $^3J_{(5\text{-OH})\text{-}(C\text{-}6)}$ = 7 Hz, ^1J = 161 Hz, C-6), 108.6 (br s, C-8), **5**; mp 97–99 °C, Found: M^+, 392.1994. $C_{25}H_{28}O_4$ requires M, 392.1988, Anal. Calcd for $C_{25}H_{28}O_4$: C, 76.50; H, 7.19. Found:C, 75.99; H, 7.35; δ_C ($CDCl_3$) 91.9 (d, ^1J = 162 Hz, C-8), 110.3 (br s, C-6), **6**; an amorphous powder, Found: M^+, 392.1994. $C_{25}H_{28}O_4$ requires M, 392.1988, δ_C 93.5 (dd, $^3J_{(5\text{-OH})\text{-}(C\text{-}6)}$ = 8Hz, ^1J = 161 Hz, C-6), 109.3 (br s, C-8).
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15. These compounds were obtained by methylation of **2**, **3**, and **1** with dimethyl sulfate, respectively.
16. The other obvious difference of the solvent effect between 6- and 8-prenylated isomers was found only on an aromatic proton of A ring as follow: between H-8 of **2** (Δ 0.06 ppm) and H-6 of **3** (Δ 0.01 ppm), H-8 of **5** (Δ 0.11 ppm) and H-6 of **6** (Δ 0.06 ppm), H-8 of **8** (Δ 0.10 ppm) and H-6 of **9** (Δ 0.05 ppm).
17. The chemical shifts of the prenyl groups [δ_H ($CDCl_3$) 1.72, 1.76 (each 3H, Me), 1.79 (6H, Me), 3.36, 4.50 (each 2H, CH_2), 5.26, 5.44 (each 1H, C=CH-)][4] were also differed from those of synthetic compounds [**5**; δ_H ($CDCl_3$) 1.67, 1.71, 1.76, 1.79 (each 3H, Me), 3.26, 4.53 (each 2H, CH_2), 5.20, 5.41 (each 1H, C=CH-), **6**; 1.62, 1.64, 1.73, 1.79 (each 3H, Me), 3.24, 4.55 (each 2H, CH_2), 5.16, 5.45 (each 1H, C=CH-)].

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