Absolute Configuration of Platyphylloside and (−)-Centrolobol

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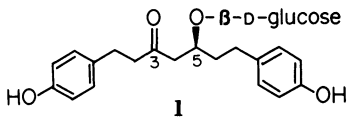
Synopsis. The absolute configuration of platyphylloside was established to be *S* by ^{13}C NMR spectroscopy. On the basis of this establishment, the *S*-configuration previously assigned to the chirality at C-3 of (−)-centrolobol was revised to the *R*-configuration.

The absolute configuration of platyphylloside, isolated from the green inner-bark of *Betula platyphylla* Sukatchev var. *japonica* (Japanese name: Shirakamba),[1] has not been assigned yet. In addition, the absolute configuration of (−)-centrolobol ($[\alpha]_D^{25}$ −8.6°) isolated from the heartwoods of *Centrolobium robustum* Mart. is assigned to be *S*[2] on the basis of the empirical rule.[3] However, this rule is not described to be applicable to the compound possessing a phenyl group. This suspicious point necessitated the reexamination of the absolute configuration of (−)-centrolobol, 1,7-bis(4-hydroxyphenyl)-3-heptanol (**5**). We now have established the absolute configuration of platyphylloside by ^{13}C NMR spectroscopy, and this establishment has resulted in the revision of the absolute configuration previously assigned to the (−)-centrolobol.

Results and Discussion

A diarylheptanoid glycoside (**1**) was isolated from the green bark of *B. platyphylla* var. *japonica*. Hydrolysis of **1** with Taka-diastase[4] gave its aglycone (**2**) and glucose. Not only the mp and spectral data (UV, IR, and ^{1}H NMR) of **1** and **2** but also the chemical behaviors of **1** and the EI-MS spectral data of **2** were identical with those reported for platyphylloside and its aglycone, respectively.[1] The glycoside (**1**) was thus confirmed to be platyphylloside, *i.e.*, 1,7-bis-(4-hydroxyphenyl)-5-(β-D-glucopyranosyloxy)-3-heptanone. Although the platyphylloside has an asymmetric carbon, however, even the optical rotation, needless to mention the absolute configuration, is not been given in Ref. 1.



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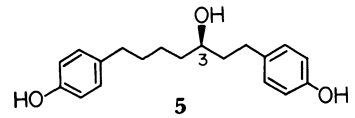

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The absolute configuration of **1** was established by ^{13}C NMR spectroscopy. On comparison of the ^{13}C NMR chemical shifts of **1** with those of **2**, the larger glycosidation shift (−2.9 ppm) at C-4 than that (−2.3 ppm) at C-6 was observed, as shown in Table 1. Application of the glycosidation shift rule[5] to these shifts indicated the configuration at C-5 of **1** and **2** to be *S*. The validity of this application has been recently confirmed for diarylheptanoid analogs.[6] The similar glycosidation shifts (Table 1) were further observed in comparison of the chemical shifts at C-4 and C-6 of the dimethyl ether (**3**) of **1** with the shifts at those of its aglycone (**4**). This observation supports the *S*-configuration at C-5 of **1** and **2**.

Table 1. ^{13}C chemical shifts (δ_c) of **1**—**4** in C_5D_5N

Carbon No.	1	2	3	4
1	28.8	28.9	28.6	28.7
2	45.5	45.5	45.3	45.4
3	208.8	209.3	208.4	208.9
4	47.8	50.7	47.8	50.9
5	75.0	67.0	75.0	66.8
6	37.6	39.9	37.4	40.0
7	30.7	31.3	30.4	31.2
1′	131.6	131.8	133.3	133.5
1″	132.6	132.8	133.5	134.1
2′	129.5	129.5	129.4	129.4
2″	129.5	129.5	129.4	129.4
3′	115.7	115.8	113.8	114.0
3″	115.7	115.8	113.8	114.0
4′	156.3	156.6[a]	157.9	158.1
4″	156.3	156.4[a]	157.9	158.1
5′	115.7	115.8	113.8	114.0
5″	115.7	115.8	113.8	114.0
6′	129.5	129.5	129.4	129.4
6″	129.5	129.5	129.4	129.4
-OMe			54.9×2	54.9×2
Sugar moiety				
1	102.9		102.7	
2	74.4		74.4	
3	77.7[a]		77.5[a]	
4	71.2		71.0	
5	77.3[a]		77.0[a]	
6	62.3		62.3	

a) These values in any vertical column may be reversed although those given here are preferred.

Compound (**5**), 1,7-bis(4-hydroxyphenyl)-3-heptanol ($[\alpha]_D^{25}$ −8.3°±0.6°), was derived from **2** by conversion of the carbonyl group into the methylene. Thus, the configuration at C-3 of **5** should be *R*. This was supported by the fact that (*R*)-1,7-bis(3,4-dimethoxyphenyl)-3-heptanol (**6**) and (*R*)-1,7-diphenyl-3-heptanol (**7**) were all levorotatory. The physical (mp and $[\alpha]_D$) and spectral (UV, IR, ^{1}H NMR, and EI-MS) data of **5** were identical with those given for (−)-centrolobol,[2] except for the assignment of absolute configuration. Consequently, the *S*-configuration previously assigned to (−)-centrolobol[2] should be revised to the *R*-configuration.

Experimental

The ^{1}H NMR spectra were taken on Hitachi R-600 FT and R-24B NMR spectrometers using TMS as an internal standard. The ^{13}C NMR spectra were obtained on a Hitachi R-42 FT NMR spectrometer (22.6 MHz; δ_{TMS}=0). The EI-MS were obtained on a Shimadzu QP-1000 mass spectrometer at 70 eV. The FD-MS was taken on a JEOL JMS-D 300 mass spectrometer equipped with a silicone emitter; the emitter current was 0—25 mA. The optical rotations were measured on a JASCO DIP-360 Digital Polarimeter using 1-dm cell. Preparative TLC was carried out on a silica-gel plate (Merck 60 GF_{254}; 0.75 mm thick).

Isolation of Diarylheptanoid Glycoside (1). According to the method described in the literature,[1] the glycoside (**1**) (1.624 g) was isolated from the green bark (10.0 kg) of *B. platyphylla* var. *japonica* and it showed the following physical and spectral data: mp 62—64°C (an amorphous solid) (lit,[1] an amorphous solid,* mp 65°C); $[\alpha]_D^{25}$ −14.3°±0.1° (*c* 2.30, MeOH); UV (EtOH) 224 (log ε 4.15), 279 nm (3.54); IR (KBr) ν_{max} 3400 (OH), 1700 (C=O), 1612, 1592, 1515 cm^{-1} (aromatic ring); ^{1}H NMR (CD_3OD) δ=1.57—2.00 (2H, m, $-CH_2-$), 2.43—2.80 (8H, m, $-CH_2-$×4), 4.31 (1H, d, *J*=7 Hz, anomeric H), 6.59—7.06 (8H, AA'BB'-type, *J*=8 and 2 Hz, aromatic H); FD-MS *m/z* 499 (M^++Na), 477 (M^++H), 476 (M^+), 296 (M^+−180).

Hydrolysis of 1 with Taka-diastase. To a solution of **1** (191 mg) in H_2O (7.5 cm^3), Taka-diastase (Sankyo Co. Ltd.,[4] 600 mg) dissolved in H_2O (15 cm^3) and then toluene (0.5 cm^3) were added. The reaction mixture was incubated at 33°C for 2 d and extracted with *n*-BuOH. An extract, after removal of the solvent, was purified by preparative TLC with a MeOH–$CHCl_3$–H_2O (10:40:1 v/v) mixture to give 1,7-bis(4-hydroxyphenyl)-5-hydroxy-3-heptanone (**2**) (55 mg): mp 127—129°C (lit,[1] 125—127°C); $[\alpha]_D^{25}$ −1.8°±0.2° (*c* 1.02, MeOH); UV (EtOH) 225 (log ε 4.13), 279 nm (3.52); IR (KBr) ν_{max} 3450, 3340 (OH), 1692 cm^{-1} (C=O); ^{1}H NMR (CD_3OD) δ=3.99 (1H, quin, *J*=6 Hz, >C<u>H</u>OH); EI-MS *m/z* 314 (M^+), 296 (M^+-H_2O). The aqueous liquor obtained in the hydrolysis was lyophilized. A residual substance obtained was acetylated with acetic anhydride–pyridine to give penta-*O*-acetylglucopyranose, which was identified by co-TLC with an authentic sample.

Methylation of 1 and Hydrolysis of Its Dimethyl Ether (3). Methylation of **1** (1.114 g) in MeOH with CH_2N_2 at 0°C gave 1,7-bis(4-methoxyphenyl)-5-(β-D-glucopyranosyloxy)-3-heptanone (**3**) (380 mg): $[\alpha]_D^{25}$ −7.4°±0.1° (*c* 1.57, MeOH). Hydrolysis of **3** (145 mg) with Taka-diastase (900 mg) in the same way as in the case of **1** gave the aglycone (**4**) (26 mg): mp 77—78°C; $[\alpha]_D^{25}$ −7.6°±0.7° (*c* 0.28, MeOH); IR (KBr) ν_{max} 3420 (OH), 1700 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ=3.77 (6H, s, $-OCH_3$×2), 4.03 (1H, quin, *J*=6 Hz, >C<u>H</u>OH).

Conversion of 2 to Diarylheptanol (5). Following the method described in the literature,[7] reduction of the carbonyl group of **2** (24 mg) with $TsNHNH_2$ (15 mg) and $NaBH_4$ (100 mg) in MeOH gave compound (**5**) (9 mg): mp 125—126°C (lit,[2] mp 128—130°C); $[\alpha]_D^{25}$ −8.3°±0.6° (*c* 0.34, MeOH); UV (MeOH) 224 (log ε 4.15), 279 (3.59), 285 nm (sh, 3.52); IR (KBr) ν_{max} 3545—3200 (OH), 1615, 1597, 1512 cm^{-1} (aromatic ring); ^{1}H NMR ($(CD_3)_2CO$) δ=1.29—1.76 (8H, m, $-CH_2-$×4), 2.29—2.72 (4H, m, $-CH_2-$×2), 3.31 (1H, brs, OH), 3.52 (1H, m, >C<u>H</u>OH), 6.66—7.11 (8H, AA'BB'-type, *J*=8 and 2 Hz, aromatic H), 7.92 (2H, brs, Ar-OH×2); EI-MS *m/z* 300 (M^+), 282 (M^+-H_2O). Found: C, 76.11; H, 8.12%. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05%.

Preparation of Diarylheptanols (6 and 7). (*S*)-1,7-bis(3,4-Dimethoxyphenyl)-5-hydroxy-3-heptanone (**8**)[6] and (*S*)-1,7-diphenyl-5-hydroxy-3-heptanone (**9**)[8] were converted to their corresponding diarylheptanols (**6** and **7**) in the same way as in the case of **2**. The structures of **6** [mp 63—65°C; $[\alpha]_D^{25}$ −6.0°±2.0° (*c* 0.20, MeOH)] and **7** [mp 44—46°C; $[\alpha]_D^{25}$ −5.7°±2.9° (*c* 0.14, MeOH)] were confirmed by their IR, ^{1}H NMR, and EI-MS spectra.

*It is described[1] that recrystallization of this amorphous solid from EtOH–H_2O gave crystals with mp 189—190°C. However, our attempt at recrystallization failed.

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