The Absolute Configuration of 4,6-Decadiyne-1,3,8-triol Isolated from *Gymnopilus spectabilis*

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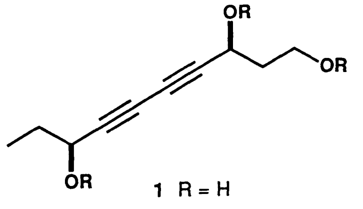
Synopsis. The absolute configuration of 4,6-decadiyne-1,3,8-triol, isolated from *Gymnopilus spectabilis*, was established as (3*S*,8*S*) by the comparison of degradated compounds with synthetic ones.

A toxic mushroom *Gymnopilus spectabilis* has been widely known for unique and curious biological activity in Japan. It has been said if you would eat it erroneously, you should laugh out loudly and could not stop doing. Therefore, the mushroom was named "Big laughter mushroom" (Ohwaraitake in Japanese). Chemical constituents of this mushroom have been studied by two groups, Matsumoto's[1] and Nozoe's,[2,3] and they reported previously isolations and structural elucidations of bitter principles, gymnopilines, gymnoprenols[1,2] and 4,6-decadiyne-1,3,8-triol (**1**).[3] Now we wish to describe absolute configuration of compound **1**.

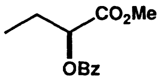
Decadiynetriol **1**, which was newly extracted from the mushroom, was converted to tribenzoate **2** in 78% yield and then ozonolysis of **2** was performed. After decomposition of the ozonide with hydrogen peroxide, the products were treated with diazomethane to give a mixture of two esters which was separated on silica-gel TLC plate developed by 20% ether-hexane to afford methyl 2-benzoyloxybutyrate (**3**) (R_f=0.45, $[\alpha]^{21}_{D}$ −1.7° (*c* 0.80, $CHCl_3$), $\Delta\varepsilon^{24}_{228}$ +5.0 (*c* 4.5×10^{-4} mol l^{-1}, MeOH)) and methyl 2,4-bis(benzoyloxy)butyrate (**4**) (R_f=0.30, $[\alpha]^{21}_{D}$ −20° (*c* 1.2, $CHCl_3$)) in 36 and 45% yield, respectively. On the other hand, they were also prepared from commercially available and optically active compounds. Through a known procedure,[4] (*S*)-(+)-2-aminobutyric acid was converted in 44% yield to hydroxy ester **5**, and it was benzoylated to give methyl (2*S*)-(−)-2-benzoyloxybutyrate (**3′**) ($[\alpha]^{22}_{D}$ −1.5° (*c* 1.6, $CHCl_3$), $\Delta\varepsilon^{24}_{228}$ +4.4 (3.4×10^{-4} mol l^{-1}, MeOH)) in 63% yield. Acetonide **6**, synthesized from (*S*)-(−)-malic acid in 47% yield by also known method,[5] was subjected to the following sequential reactions: i) reduction with borane dimethyl sulfide complex, ii) benzoylation of hydroxyl group, iii) removal of acetonide protective group under acidic conditions, iv) esterification with CH_2N_2, v) benzoylation of hydroxyl group, to yield methyl (2*S*)-2,4-bis(benzoyloxy)-butyrate (**4′**) ($[\alpha]^{23}_{D}$ −21° (*c* 1.0, $CHCl_3$)) was obtained in 65% over all yield. Both synthetic products **3′** and **4′** were identical with degradation products **3** and **4**, respectively, on spectral data (NMR, IR, and MS) including optical rotation and chromatographic behavior. Absolute configurations of both **3** and **4** were thus represented as *S*. Accordingly the stereochemistry of the natural product **1** should be assigned to 3*S* and 8*S* configurations.

Experimental

Melting point was uncorrected. All ^{1}H NMR spectra were measured on a Hitachi R-90H spectrometer in $CDCl_3$, and ^{13}C NMR spectrum was determined on a JEOL JNM-GX 270 spectrometer in CD_3OD. IR spectra were recorded



1 R = H
2 R = Bz



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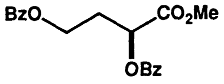

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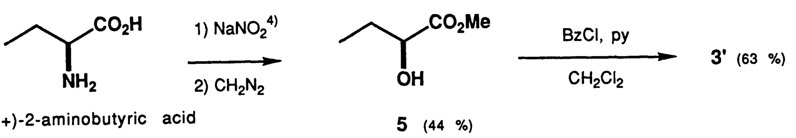

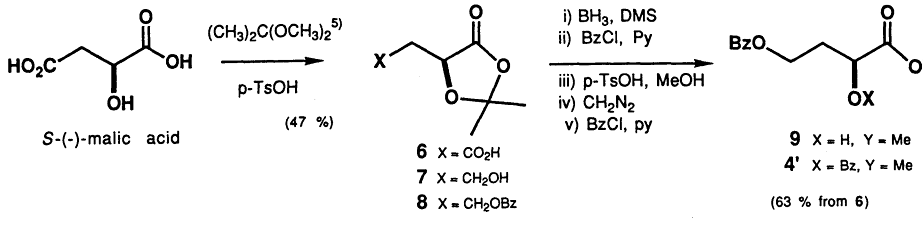

on a JASCO IR-S spectrophotometer. Optical rotations were obtained by JASCO DIP-360 digital polarimeter, and CD spectra by JASCO J-20A automatic recording spectropolarimeter. High and low mass spectra were recorded on a JEOL JMS-DX 303 spectrometer.

4,6-Decadiyne-1,3,8-triol (1).[3] The mushroom, Gymnopilus spectabilis, was collected in Aomori prefecture and **1** was isolated as colorless oil in 0.027% from fresh fruit bodies: $[\alpha]_D^{23}$ −5.8° (*c* 1.7, MeOH); ^{13}C NMR δ=9.76 (q), 31.72 (t), 41.30 (t), 59.05 (t), 60.20 (d), 64.31 (d), 68.93 (s), 69.09 (s), 81.25 (s), and 81.61 (s); FD-MS *m/z* 183 ($M^+ + H$) and 165 (($M^+ H - H_2O$), base peak).

(3*S*,8*S*)-1,3,8-Trisbenzoyloxy-4,6-decadiyne (2). 4,6-Decadiynetriol **1** (9.0 mg, 0.049 mmol) was treated with pyridine (0.20 ml) and benzoyl chloride (50 mg, 0.35 mmol) in dichloromethane (0.50 ml). After 6 h stirring, the mixture was poured into 0.5% citric acid solution and extracted with ether. The ethereal solution was washed with brine, dried (Na_2SO_4) and concentrated. Chromatography of the obtained oil on silica gel (2 g) with 50% hexane–ether gave tribenzoate **2** as amorphous solid (19 mg, 0.038 mmol, 78%): mp 97—102 °C; $[\alpha]_D^{21}$ +4.70° (*c* 1.7, $CHCl_3$); ^1H NMR δ=1.07 (3H, t, *J*=7 Hz), 1.94 (2H, quint, *J*=7 Hz), 2.38 (2H, q, *J*=6 Hz), 4.54 (2H, t, *J*=7 Hz), 5.59 (1H, t, *J*=7 Hz), 5.88 (1H, t, *J*=6 Hz), and 7—8 (15H); IR (Nujol) 1730, 1690, 1270, 1095, and 710 cm^{-1}; EI-MS *m/z* 494 (M^+) and 105 ($C_6H_5CO^+$, base peak); Found: *m/z* 494.1777, Calcd for $C_{31}H_{26}O_6$: M, 494.1730.

Oxidative Degradatioon of 1,3,8-Trisbenzoyloxy-4,6-decadiyne (2). To a dichloromethane solution (10 ml) of tribenzoate **2** (40 mg, 0.080 mmol), ozone gas was bubbled for 20 min at 0 °C. After removal of excess ozone by bubbling of oxygen, 30% hydrogen peroxide (0.10 ml) was added and the mixture was stirred for 20 min to decompose the ozonide product. Dimethyl sulfide (2.0 ml) was added to decompose excess peroxide. The solvent was removed and an obtained oil was diluted with methanol (10 ml). An ethereal solution of diazomethane was added until yellow color did not disappear. The mixture was diluted with ether, washed with water and brine, dried (Na_2SO_4) and concentrated. The purification of the oil by preparative TLC (silica gel) with 20% ether–hexane gave methyl 2-benzoyloxybutyrate (**3**) as a colorless oil (6.5 mg, 0.029 mmol, 36%) and methyl 2,4-bis(benzoyloxy)butyrate (**4**) as a colorless oil (13 mg, 0.036 mmol, 45%).

Methyl 2-Benzoyloxybutyrate (3): R_f=0.45 (silica gel, 20% ether–hexane); $[\alpha]_D^{21}$ −1.7° (*c* 0.80, $CHCl_3$) $\Delta\varepsilon_{228}^{24}$ +5.0 (*c* 4.5×10^{-4} mol l^{-1}, MeOH); ^1H NMR δ=1.09 (3H, t, *J*=7 Hz), 2.02 (2H, dq, *J*=6 and 7 Hz), 3.77 (3H, s), 5.21 (1H, t, *J*=6 Hz), 7.5 (3H, m), and 8.0 (2H, m); IR (film) 1760, 1730, 1115, and 715 cm^{-1}; EI-MS *m/z* 222 (M^+) and 105 ($C_6H_5CO^+$, base peak); Found: *m/z* 222.0887, Calcd for $C_{12}H_{14}O_4$: M, 222.0892.

Methyl 2,4-Bis(benzoyloxy)butyrate (4): R_f=0.30 (silica gel, 20% ether–haxane); $[\alpha]_D^{21}$ −21° (*c* 1.2, $CHCl_3$); ^1H NMR δ=2.48 (2H, q, *J*=7 Hz), 3.73 (3H, s), 4.54 (2H, t, *J*=6 Hz), 5.49 (1H, t, *J*=6 Hz), 7.5 (6H, m), and 8.0 (4H, m); IR (film) 1760, 1730, 1605, 765, and 715 cm^{-1}; EI-MS *m/z* 342 (M^+), 310 ($M^+ - MeOH$), and 105 ($C_6H_5CO^+$, base peak); Found *m/z* 342.1102, Calcd for $C_{19}H_{18}O_6$: M, 342.1103.

Methyl (2*S*)-2-Benzoyloxybutyrate (3′). A solution of methyl (2*S*)-2-hydroxybutyrate (**5**) (43 mg, 0.41 mmol), pyridine (0.20 ml), and benzoyl chloride (60 mg, 0.43 mmol) in dichloromethane (1.0 ml) was stirred at room temperature for 10 h. The mixture was poured into water and extracted with ether. The organic layer was washed with brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue on silica gel (3 g) with 15% ether–hexane gave benzoate **3′** as a colorless oil (68 mg, 63%); $[\alpha]_D^{22}$ −1.5° (*c* 1.6, $CHCl_3$), $\Delta\varepsilon_{228}^{24}$ +4.4 (3.4×10^{-4} mol l^{-1}, MeOH); Found: *m/z* 222.0905, Calcd for $C_{12}H_{14}O_4$: M, 222.0892.

Methyl (2*S*)-2,4-Bis(benzoyloxy)butyrate (4′). Borane dimethyl sulfide complex (2.0 ml, 21 mmol) was added to THF solution (50 ml) of (3S)-3,4-*O*-isopropyliden-4-oxobutyric acid (**6**) (1.0 g, 5.7 mmol) at 0 °C. After 5 h stirring, methanol was added slowly to decompose excess hydride. The mixture was poured into brine and extracted with chloroform. The organic solution was dried (Na_2SO_4), concentrated to afford an alcohol **7** (870 mg, 5.3 mmol, 93%): ^1H NMR δ=1.52, 1.65 (each 3H, s), 2.00 (2H, q, *J*=6 Hz), 2.31 (1H, brs), 3.81 (2H, s, *J*=6 Hz), and 4.55 (1H, dd, *J*=6 and 8 Hz).

To the dichloromethane solution (10 ml) of the alcohol **7** (870 mg, 5.3 mmol), pyridine (0.80 ml, 10 mmol) and benzoyl chloride (1.0 g, 7.1 mmol) were added at 0 °C. The mixture was allowed to warm to room temperature and was stirred for 12 h. The mixture was poured into water and extracted with ether. The ethereal solution was washed with brine, dried (Na_2SO_4), and concentrated to give a benzoyl ester **8** (1.3 g, 5.0 mmol, 94%): ^1H NMR δ=1.53, 1.57 (each 3H, s), 2.27 (2H, m), 4.50 (3H, m), 7.1—7.7 (3H), and 7.9—8.2 (2H).

The ester **8** (1.3 g, 5.0 mmol) was treated with *p*-TsOH (10 mg) in methanol (15 ml) for 10 h. To this solution, ethereal solution of diazomethane was added until yellow color did not disappear, and the solvent was removed to yield ester **9**: ^1H NMR δ=2.23 (2H, m), 2.92 (1H, brs), 3.24 (3H, s), 4.54 (2H, m), 7.2—7.6 (3H), and 7.9—8.2 (2H). The obtained ester **9** was stirred with benzoyl chloride (1.0 ml, 7.1 mmol) and pyridine (0.80 ml, 10 mmol) in dichloromethane (15 ml) at room temperature for 10 h. The mixture was poured into water and extracted with ether. The ethereal solution was washed with sat. $CuSO_4$ aqueous solution and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue on 40 g of silica gel with 25% ether–hexane gave 2,4-bis(benzoyloxy)butyrate **4′** as a colorless oil (1.3 g, 3.7 mmol, 74% through 2 steps): $[\alpha]_D^{23}$ −21° (*c* 1.0, $CHCl_3$); Found: *m/z* 342.1094, Calcd for $C_{12}H_{14}O_4$: M, 342.1103.

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