SHORT COMMUNICATION



Determination of the absolute stereochemistry of (+)-solaniol

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Abstract

The absolute stereochemistry of (+)-solaniol (5,8-dihydroxy-7-(2-hydroxypropyl)-2-methoxy-6-methyl-1,4-naphthoquinone) (1) was deduced to be *S* using Mosher's method. Our result did not accord with the *R* configuration of (+)-solaniol recently proposed by Maharjan et al., but agreed with the *S* configuration determined by X-ray crystallographic analysis by Kyekyeku et al. In addition, complete and unambiguous assignments of 13 C NMR signals for 1 are reported.

Graphic abstract



Keywords Solaniol · Absolute stereochemistry · Mosher's method · Naphthoquinone

A naphthoquinone derivative, (+)-solaniol (5,8-dihydroxy-7-(2-hydroxypropyl)-2-methoxy-6-methyl-1,4-naphthoquinone) (1) ($[\alpha]_D^{25}$ +122 (c, 0.053 in MeOH)) was first isolated from *Fusarium solani* D₂ purple (Arsenault 1968). Subsequently, solaniol has been reported from several fungi

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² School of Agriculture, Meiji University, Kawasaki, Kanagawa 214-8571, Japan such as *Fusarium* sp. (Kimura et al. 1988). We recently isolated (+)-solaniol ($[\alpha]_D^{25}$ +121 (c, 0.048, MeOH)) from the endophytic fungus *Phialemonium curvatum* (Rathnayake et al. 2018) and *Monacrosporium ambrosium*, the ectosymbiotic fungus of tea shot-hole borer *Euwallacea fornicates* (Kehelpannala et al. 2018). The absolute stereochemistry of (+)-solaniol was determined to be *S* by X-ray crystallographic analysis as shown in Fig. 1 (Kyekyeku et al. 2017). Quite recently, Maharjan et al. reported the isolation of (+)-solaniol ($[\alpha]_D^{25}$ +25 (c 0.1, MeOH)) from an endophytic *Fusarium* sp. and proposed that (+)-solaniol has *R* configuration by comparing measured specific rotation with calculated value (Maharjan et al. 2020). This inconsistent stereochemical assignment of **1** prompted us to report our independent result on the absolute configuration of

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Fig. 1 Structure of compound 1

Table 1. 1 H (500 MHz) and 13 C (125 MHz) NMR data for compound **1** (CDCl₃)

Position	δ_{C}	$\delta_{\rm H}$, mult. (<i>J</i> in Hz)
1	177.5	_
2	160.4	-
3	109.4	6.15, s
4	184.0	-
4a	107.8	-
5	160.7	-
6	142.4	-
7	138.5	-
8	162.4	-
8a	109.4	-
9	36.2	2.93, m
10	67.6	4.17, m
11	23.9	1.34, d (6.3)
12	13.0	2.35, s
2-OCH ₃	56.7	3.91, s
5-OH		13.31, s
8-OH		12.99, s
10-OH		2.15, brs

(+)-solaniol (1), which was determined by Mosher's method (Ohtani et al. 1991). In addition, the complete 13 C signal assignments of 1 on the basis of HMBC correlations are reported in Table. 1.

To apply the advanced Mosher ester method (Ohtani et al., 1991), the required (S)- and (R)- α -methoxy- α -(trifluoromethyl)phenyl acetyl (MTPA) ester derivatives (1S and $(1\mathbf{R})$ were prepared from (+)-solaniol (Fig. 2), which was obtained from Monacrosporium ambrosium (Kehelpannala et al. 2018), by reacting 1 with (R)-MTPA and (S)-MTPA chlorides, respectively. The reaction furnished mono-MTPA ester in good yield with the use of slightly less than two equivalents of the acid chloride since the chelated C-5 and C-8 phenol groups were less reactive than the C-10 hydroxyl group. The $\Delta(\delta S - \delta R)$ values for 1S and 1R are listed in Fig. 2. The value of 11-H₃ is negative, whereas those values for the protons of the other side of the carbinol center are positive with the exception of C-2-OCH₃. Thus, the configuration of the carbinol center of 1 was unambiguously determined to be S according to the rule of Mosher's method (Ohtani et al. 1991; Hoye et al. 2007). If the carbinol center has R configuration, the $\Delta(\delta S - \delta R)$ value for 11-H₃ should be positive and the values for the other protons should be negative. Our result confirmed the correctness of the stereochemical assignment by X-ray crystallographic analysis. This implies that the methodology employed by Maharjan's group that is based on comparing measured specific rotation with calculated value lacks credibility.

We previously reported the ¹H and ¹³C NMR data of **1** (Rathnayaka et al. 2018). The ¹³C NMR data reported by Maharjan's group for **1** (Maharjan et al. 2020) differed from ours in several signals. Therefore, the ¹³C signal assignments were reinvestigated based on 2D NMR study. The observed



Fig. 2 Preparation of (*S*)- and (*R*)-MTPA esters (1S and 1R) of 1, and $\Delta(\delta S - \delta R)$ values (ppm) for 1S and 1R



Fig. 3 HMBC correlations $(H \rightarrow C)$

HMBC correlations are shown in Fig. 3, which fully confirmed the correctness of our previous assignments. Complete and unambiguous assignments of the 13 C NMR signals of 1 are listed in Table 1.

In conclusion, the *S* configuration of (+)-solaniol was determined by Mosher's method, which was consistent with the result by X-ray crystallographic analysis, but not consistent with the result of Maharjan's group. To our knowledge, the enantiomer of (+)-(S)-solaniol has not been reported as a natural compound so far.

¹H and ¹³C NMR spectra were recorded on a Bruker DRX 500 (500 MHz for ¹H and 125 MHz for ¹³C) or JEOL JMN-AL300 (300 MHz for ¹H and 75 MHz for ¹³C) spectrometer in CDCl₃ solution. ESI mass spectra were measured on an Exactive Orbitrap mass spectrometer (Thermo Fisher Scientific). Optical rotations were measured on a JASCO P-2200 polarimeter. Preparative TLC was performed using Merck precoated Si gel 60 F254 glass plates, and spots were detected under UV lump (254 nm).

Preparation of (S)- and (R)-MTPA esters (1S and 1R)

(+)-Solaniol (1) (2.2 mg, 7.5 µmol) in pyridine (50 µL) was treated with (*R*)-(–)-MTPA chloride (2.5 µL, 13.4 µmol) at room temperature with occasional shaking by hand. After 30 min, the solvent was evaporated under reduced pressure. The residue was subjected to preparative TLC (developed with hexane–EtOAc 2:1, two times) to afford (*S*)-MTPA ester (**1S**) (2.0 mg): yellow oil, ESI–MS m/z, 507 [M-H][–], ¹H NMR (CDCl₃, 300 MHz): δ 13.27 (1H, s, 5-OH), 12.95 (1H, brs, 8-OH), 7.37–7.23 (5H, m, phenyl-H₅), 6.22 (1H, s, H-3), 5.45 (1H, m, 10-H), 3.95 (3H, s, 2-OCH₃), 3.33 (3H, s, OCH₃ of MTPA), 3.07 (2H, m, 9-H₂), 2.18 (3H, s, 12-H₃), 1.41 (3H, d, J=6.3 Hz, 11-H₃).

(+)-Solaniol (1) (2.2 mg, 7.5 μmol) in pyridine (50 μL) was similarly reacted with (*S*)-(+)-MTPA chloride (2.5 μL, 13.4 μmol). Purification of the crude product by preparative TLC to afford (*R*)-MTPA ester (1**R**): yellow oil, ESI-MS m/z 507 [M-H]⁻, ¹H NMR (CDCl₃, 300 MHz): δ 13.14 (1H, s, 5-OH), 12.91 (1H, brs, 8-OH), 7.26–7.12 (5H, m, phenyl-H₅), 6.21 (1H, s, H-3), 5.44 (1H, m, 10-H), 3.96 (3H, s, 2-OCH₃), 3.57 (3H, s, OCH₃ of MTPA), 2.99 (2H, m, 9-H₂), 2.03 (3H, s, 12-H₃), 1.50 (3H, d, J=6.3 Hz, 11-H₃).

Compliance with ethical standards

Conflict of interest No potential conflict of interest was reported by the authors.

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