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Isolation and Structure of Magnoloside A, a New Phenylpropanoid Glycoside from Magnolia obovata Thunb.

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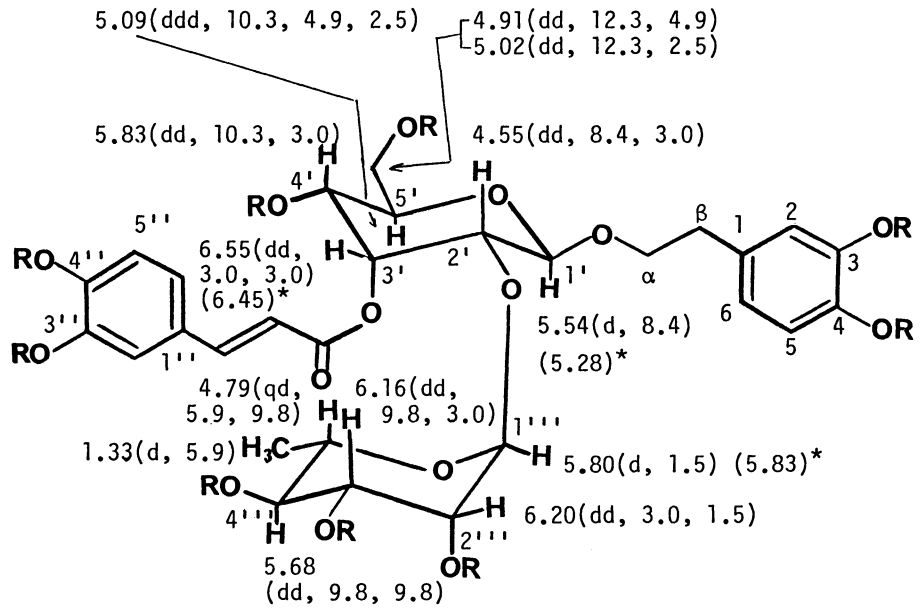
Magnoloside A, a novel phenylpropanoid glycoside has been isolated from the MeOH extract of Magnolia obovata and its structure has been elucidated as 3,4-dihydroxy-β-phenyl-ethyl-O-α-L-rhamnopyranosyl-(1→2)-3-O-caffeoyl-β-D-allopyranoside by means of spectroscopic and chemical evidences.

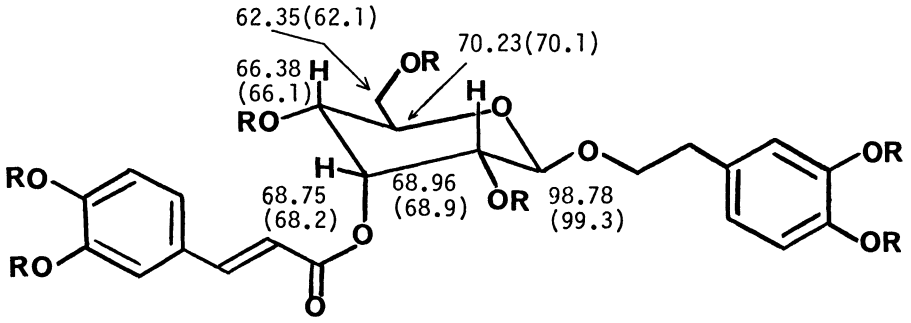
Japanese traditional medicine, the dried bark of Magnolia obovata Thunb. has been prescribed along with the other drugs for neurosis and gastrointentinal complains,[1] and elaborates a large amount of neolignans, honokiol and magnolol.[2] Also, these biphenyl compounds were reported to exhibit various physiological responses in vitro and in vivo.[3] As a part of our continuing search for pharmacological active substances from natural sources,[4] we investigated polar constituents in the title plant, and consequently could isolate a new phenolic glycoside 1 named magnoloside A, which contained a rarely occurred allopyranose as inner sugar moiety. This paper deals with the isolation and structure elucidation of magnoloside A (1).

The MeOH extract of M. obovata was partitioned between n-BuOH and H_2O. The n-BuOH soluble portion (150 g) was subjected to repeated silica gel and finally HW-40F chromatographies to yield 2.98 g of magnoloside A (1) as a colorless powder: $[\alpha]_D^{18}$ -36.8 (c 0.82, EtOH); IR (KBr) 3400 (OH), 1700 (conjugated ester), 1630 (C=C), 1603 and 1520 cm^{-1} (aromatic); UV (EtOH) 217 (ε 15600), 220 (ε 8100), 290 (ε 9900), and 330 nm (ε 13500). The FABMS exhibited molecular ion peaks due to $[M + H]^+$ at m/z 625 and $[M + Na]^+$ at m/z 647. The ^1H NMR and ^{13}C NMR spectra[5] showed 1 to have two aromatic [δ 6.77 (dd, J = 7.7, 1.7 Hz), 7.17 (d, J = 7.7 Hz), and 7.25 (d, J = 1.7 Hz); δ 6.67 (d, J = 15.5 Hz), 7.91 (d, J = 15.5 Hz), 7.05 (d, J = 7.7, 1.7 Hz), 7.18 (d, J = 7.7 Hz), and 7.48 (d, J = 1.7 Hz)], and two sugar moieties [δ 5.28 (d, J = 7.7 Hz) and 5.83 (bs)]. Acetylation of 1 with Ac_2O/pyr. overnight led to a fully acetylated derivative (3),[6] m/z 1002 $[M]^+$, the ^1H NMR spectrum of which revealed the presence of five aliphatic acyl signals (δ 1.93, 1.98, 1.99, and 2.09) and four aromatic acyl signals (δ 2.26, 2.27, 2.30, and 2.31). Mild hydrolysis of 1 in refluxing aqueous 0.1 M HCl for 3 h yielded compound (4) and L-rhamnose[7] as the only detectable sugar, suggesting its position to be the terminal unit. In addition, further evidences of the terminal rhamnose moiety was obtained from the observation of pertinent fragment ion peak at m/z 147



1 : R = H
2 : R = $COCF_3$
3 : R = Ac

Fig. 1. Magnoloside A pertrifluoroacetate (2): Pertinent ^1H NMR (400 MHz, pyridine-d_5) signals are shown; * are chemical shifts in magnoloside A (1).



4 : R = H
5 : R = Ac

Fig. 2. ^{13}C NMR data (62.9 MHz, $CDCl_3$) for 5. Chemical shifts of methyl-2,3,4,6-tetraacetyl-β-D-allopyranose are given in parentheses.

in the EIMS. Treatment of 4 with NaOMe/MeOH at room temperature furnished methyl caffeate, the detection of which indicated 1 to contain a caffeoyl group. Pertrifluoroacetate (2) was readily prepared in a NMR tube by adding a few drops of $(CF_3CO)_2O$ into a pyridine-d_5 solution of 1 and standing for 10 min, and then was directly subjected to ^1H NMR measurement. Detailed proton decoupling experiments (Fig. 1) of 2 disclosed the presence of allopyranose as the inner sugar unit and rhamnose as the terminal sugar, as well as of 3,4-dihydroxyphenylethyl and caffeoyl groups. Moreover, the presence of the allopyranose unit was substantiated by good accordance of the ^{13}C NMR data for peracetate (5) with those of methyl-2,3,4,6-tetraacetyl-β-D-allopyranose[11] as shown in Fig. 2. This trifluoroacetylation caused the signals due to H-4', 5', and 6' in the allose unit and all the protons signals corresponding to the terminal rhamnose moiety (except for H-1''' and 6''') downfield shifted, but did not largely effect the H-1', 2', and 3' signals in the allose. These results implied that the OH groups attached at C-1', 2', and 3' on the inner allose should be substituted, and the caffeoyl group must be connected to the C-3' position through an ester linkage in consideration of the chemical shift values for H-3' (δ 6.43 for 1 and 6.55 for 2). On the other hand, the linkage position of the terminal rhamnose could be clarified by comparison of the ^1H NMR data for the peracetate (3) with those of 5, in particular, on the regional signals due to the inner allose (Table 1). Namely, the H-2' signals of 5 was appeared at lower field by + 1.22 ppm than the corresponding one in 3, whereas the remaining signals were found to be in good accordance to each other. This fact clearly indicated that the terminal rhamnose should be bonded to C-2' on the inner allose unit, and thus the 3,4-dihydroxyphenylethyl group must be linkaged at C-1' through a glycosylation bond. Finally, it was evident from the J values (J = 7.8 Hz for H-1' and 1.5 Hz for H-1''') that anomeric configurations for allopyranose and rhamnopyranose were β and α, respectively. Accordingly, the structure of magnoloside A (1) was elucidated to be 3.4-dihydroxy-β-phenyl-ethyl-O-α-L-rhamnopyranosyl-(1→2)-3-O-caffeoyl-β-D-allopyranoside.

Table 1. ^1H NMR data (400 MHz, $CDCl_3$) for the allose protons of 3 and 5

H	3	5
1'	4.79d (7.8)	4.82d (8.3)
2'	3.78dd (7.8, 3.1)	4.96dd (8.3, 3.1)
3'	5.80dd (3.1, 3.1)	5.76dd (3.1, 3.1)
4'	4.93dd (10.2, 3.1)	5.01dd (10.4, 3.1)
5'	4.2m[a)]	4.2m[a)]
6'	4.2m[a)]	4.2m[a)]

a) poorly resolved proton due to overlapping.

A large number of phenylpropanoid glycosides are known to date,[8)] and some of them are of biological and pharmacological interests.[9)] Most of them contain more than one sugar units and a substituted phenylethanol moiety, and also their sugar units comprise glucose as inner sugar core in addition to rhamnose, arabinose, or apiofuranose[9)] as terminal sugar moiety. Phenolic glycoside with allose as inner sugar unit, however, has not been so far recorded. We believe magnoloside A (1) to

be the first reported phenylpropanoid glycoside with allopyranose as inner sugar core and also no phenolic glycoside has not been detected in Magnolia obovata before this paper.

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References

1) M. Osaw, Jpn. J. Orient. Med., 4, 38 (1953).
2) M. Fujita, H. Itokawa, and Y. Sashida, Chem. Pharm. Bull., 20, 212 (1972).
3) K. Watanabe, H. Watanabe, Y. Goto, M. Yamaguchi, N. Yamamoto, and K. Hagino, Planta Med., 49, 103 (1983).
4) T. Hasegawa, Y. Fukuyama, K. Nakagawa, M. Tori, and Y. Asakawa, Chem. Lett., 1987, 329.
5) For 1 ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.67 (3 H, d, 6.0 Hz, H-6''), 3.06 (2 H, t, 7.3 Hz, H-β), 3.83 (2 H, dt, 16.7, 7.3 Hz, H-α), 4.77 (1 H, dq, 9.0, 6.0 Hz, H-5'''), 5.28 (1 H, d, 7.7 Hz, H-1'), 5.83 (1 H, bs, H-1'''), 6.45 (1 H, bs, H-3'), 6.67 (1 H, d, 15.5, H-α''), 6.77 (1 H, dd, 7.7, 1.7 Hz, H-6), 7.05 (1 H, dd, 7.7, 1.7 Hz, H-6''), 7.17 (1 H, d, 7.7 Hz, H-5), 7.18 (1 H, d, 7.7 Hz, H-5''), 7.25 (1 H, d, 1.7 Hz, H-2), 7.48 (1 H, d, 1.7 Hz, H-2''), 7.91 (1 H, d, 15.5 Hz, H-β''); ^{13}C NMR (100.18 MHz, methanol-d_4): δ 17.84 (q, 6'''), 36.68 (t, β), 62.96 (t, 6'), 67.54 (d, 4'), 69.97 (d, 5'''), 71.39 (d, 3'), 71.98 (d, 3'''), 72.09 (d, 5'), 72.46 (t, α), 73.95 (d, 4'''), 74.05 (d, 2'), 76.09 (d, 5'), 98.59 (d, 1'), 100.93 (d, 1'''), 115.47 (d, 2''), 115.61 (d,α''), 116.58 (d, 5''), 116.74 (d, 2), 117.32 (d, 5), 121.49 (d, 6), 123.03 (s, 6''), 128.09 (s, 1''), 131.98 (s, 1), 144.67 (s, 3), 146.11 (s, 4), 146.84 (s, 4''), 147.27 (d, β''), 149.61 (s, 3''), and 168.99 (s, CO).
6) 3: IR (KBr) 1750, 1640, and 1510 cm^{-1}; m/z (rel. int.) 1002 $[M]^+$ (14), 960 $[M - 42]^+$ (17), 765 $[M - 237]^+$ (56), 243 $[Ac_3$ rham$]^+$, 237 $[Ac_2$ caff$]^+$.
7) The sugars were detected in the free form by TLC [silica gel, iPrOH : EtOAc : H_2O (7 : 2 : 1), rhamnose: Rf = 0.65].
8) M. F. Lahloub, G. -A. Gross, O. Sticher, T. Winkler, and H. -R. Schulten, Planta Med., 1986, 352.
9) T. Sato, S. Kozima, and K. Kobayashi, Yakugaku Zasshi, 105, 1131 (1985).
10) R. Cooper, P. H. Solomon, I. Kubo, K. Nakanishi, J. N. Shoolery, and J. L. Occolowitz, J. Am. Chem. Soc., 102, 7953 (1980).
11) K. Block, S. R. Jensen, B. J. Nielsen, and V. Norn, Phytochemistry, 17, 753 (1978).

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