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Structure of Nigakilactone O, a New Quassinoid from Picrasma Ailanthoides

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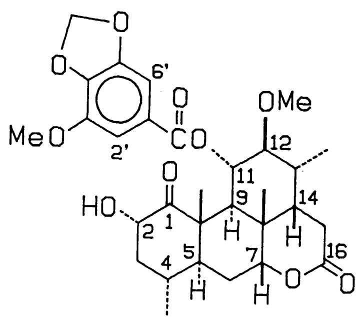
Nigakikactone O, a new picrasane-skeletal compound, was isolated from *Picrasma ailanthoides* PLANCHON, and its structure including the stereochemistry was determined to be 2α-hydroxy-12β-methoxy-11α-(3-methoxy-4,5-methylenedioxybenzoyloxy)-picrasane-1,16-dione mainly by 1D and 2D NMR techniques.

Studies on bitter principles of Simaroubaceous family have been extensively continued through almost a century.[1,2] Recently we have reinvestigated the constituents of *Picrasma ailanthoides* PLANCHON (Japanese name: nigaki) and several kinds of tirucallane-type triterpenoids have been isolated[3] together with a new quassinoid, named nigakilactone O (**1**). In this paper, we wish to report the isolation and structural elucidation of this compound (**1**), a C_{30}-compound possessing a picrasane skeleton.

Hot methanol extract of 9 kg of twigs of *P. ailanthoides* was partitioned between dichloromethane and water. The dichloromethane layer was separated by silica-gel column chromatography. Nigakilactone O (15 mg) was isolated from a fraction containing three components, two of which were known neoquassin and picrasinol B,[1] using gel permeation chromatography.

Nigakilactone O (**1**),[4] mp 207-208 °C, $[\alpha]_D^{17}$ -5.6° (c 0.39, $CHCl_3$), gave a molecular ion peak at m/z 558.2471 ($C_{30}H_{38}O_{10}$). Assignments of all the signals on ^1H and ^{13}C NMR spectra were carried out from ^1H-^1H COSY, ^1H-^{13}C COSY, and HMBC ones. For example, all the protons attached directly to the carbons of picrasane skeleton could be assigned from ^1H-^1H COSY spectrum. Remaining protons (two methoxyl protons, methylene protons (δ 6.02), and two aromatic protons) could be assigned by HMBC spectrum; an investigation on the HMBC spectrum led to not only the assignment of skeletal quaternary carbons but also the determination of the presence of 3-methoxy-4,5-methylenedioxybenzoyloxyl group[5] at C-11 position. That is, the ester carbonyl carbon signal at δ 165.3 showed only one correlation peak with a C-11 proton signal (δ 5.47) besides the aromatic protons. The presence of this aroyl group was confirmed by the spectral comparison with ethyl 3-methoxy-4,5-methylenedioxybenzoate,[6] which was prepared from ethyl gallate.[7]

Stereochemistry of **1** was deduced from ^1H-^1H spin coupling constants at 1D ^1H NMR and phase sensitive NOESY spectra. All the angular chiral centers (C-5, C-7, C-8, C-9, C-10, and C-14) together with C-4 and C-13 were compatible with the usual picrasane skeleton. A proton at C-2 (δ 4.49) was assigned as a β-axial one from the coupling constants (J=11.6 and 9.2 Hz), which was confirmed by the presence of an NOE peak with C-10β-axial methyl proton signal. As the C-11 proton showed correlation peaks with C-8 and C-10 methyl signals at the NOESY spectrum and J values between C-11H and C-9αH and between C-11H and C-12H were 11.6 and 9.2 Hz, respectively, C-11 and C-12 protons were deduced as β-axial and α-axial, respectively.



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Thus, the structure of nigakilactone O was determined as 2α-hydroxy-12β-methoxy-11α-(3-methoxy-4,5-methylenedioxybenzoyloxy)picrasane-1,16-dione. To our knowledge, this is the first example to have a large aroyl group at C-11 position of the picrasane skeleton.

References

1) Reviews: J. Polonsky, Fortschr. Chem. Org. Naturst., 47, 221 (1985).

2) On our synthetic works: H. Hirota, A. Yokoyama, K. Miyaji, T. Nakamura, and T. Takahashi, Tetrahedron Lett., 28, 435 (1987); H. Hirota and T. Takahashi, Yuki Gosei Kagaku Kyokai Shi, 45, 1199 (1987); and references cited therein.
On our structure determination works of *P. ailanthoides*: T. Murae, A. Sugie, T. Tsuyuki, and T. Takahashi, Chem. Pharm. Bull., 23, 2188 (1975); and references cited therein.

3) Unpublished result. Oral presentation: Y. Niimi, T. Tsuyuki, T. Takahashi, and K. Matsushita, the 54th National Meeting of the Chemical Society of Japan, April 1987; Abstr. No. 2ⅢL11.

4) Spectral data of 1: UV (EtOH) 282 nm (ε 7740); IR (KBr) ~3450, 1730-1710, and 1640 cm^{-1}; MS m/z 558 (M), 362 (M-196), 196, and 179 (base peak); ^{1}H NMR (400 MHz; $CDCl_3$) δ 0.86 (3H, d, J=6.5 Hz; 4α-Me), 1.01 (1H, ddd, J=12.9, 12.6, 11.0 Hz; 3α-H), 1.02 (3H, d, J=6.8 Hz; 13α-Me), 1.22 (3H, s; 10β-Me), 1.32 (3H, s; 8β-Me), 1.44 (1H, ddd, J=12.8, 11.2, 3.5 Hz; 5α-H), 1.77 (1H, m; 6β-H), ~1.8 (1H, m; 14β-H), ~1.9 (1H, m, 4β-H), 1.94 (1H, ddd, J=14.6, 3.6, 3.5 Hz; 6α-H), 2.24 (1H, dqd, J=11.0, 6.8, 5.0 Hz; 13β-H), 2.42 (1H, ddd, J=12.9, 7.7, 4.4 Hz; 3β-H), 2.59 (1H, dd, J=19.1, 12.1 Hz; 15α-H), 2.66 (1H, dd, J=19.1, 2.7 Hz; 15β-H), 2.92 (1H, d, J=11.6 Hz; 9α-H), 3.21 (1H, dd, J=11.0, 9.2 Hz; 12α-H), 3.27 (3H, s; 12β-OMe), 3.94 (3H, s; 3'-OMe), 4.20 (1H, dd, J=3.6, 2.1 Hz; 7β-H), 4.49 (1H, dd, J=11.0, 7.7 Hz; 2β-H), 5.47 (1H, dd, J=11.6, 9.2 Hz; 11β-H), 6.02 (2H, s; OCH_2O), 7.13 (1H, d, J=1.5 Hz; 6'-H), and 7.26 (1H, d, J=1.5 Hz; 2'-H). ^{13}C NMR (100 MHz; $CDCl_3$) δ 13.5 (q; 10-Me), 14.3 (q; 13-Me), 18.3 (q; 4-Me), 21.9 (q; 8-Me), 26.3 (t; C-6), 28.0 (t; C-15), 28.6 (d; C-4), 35.1 (d; C-13), 35.6 (s; C-8), 35.7 (d; C-9), 45.1 (d; C-14), 47.7 (d; C-5), 48.9 (t; C-3), 49.2 (s; C-10), 56.6 (q; 3'-OMe), 61.0 (q; 12-OMe), 69.9 (d; C-2), 73.3 (d; C-11), 82.4 (d; C-7), 85.5 (d; C-12), 102.3 (t; OCH_2O), 104.1 (d; C-6'), 110.4 (d; C-2'), 123.7 (s; C-1'); 139.9 (s; C-4'), 143.3 (s; C-3'), 148.8 (s; C-5'), 165.3 (s; ester carbonyl), 170.0 (s; C-16), and 214.6 (s; C-1).

5) Several kinds of natural compounds having this aroyl group have already been known. e.g.) Veneserpine: A. Chatterjee, P. L. Majumder, and B. C. Das, Chem. Ind., 1969, 1388. Echitoserpine: P. L. Majumder, B. N. Dinda, A. Chatterjee, and B. C. Das, Tetrahedron, 30, 2761 (1974). Pallinin: A. Y. Kushmuradov, A. I. Saidkhodzhaev, and V. M. Mālikov, Khim. Prir. Soedin., 1986, 53.

6) Spectral data of ethyl 3-methoxy-4,5-methylenedioxybenzoate: UV (EtOH) 278 nm (ε 9090); ^{1}H NMR ($CDCl_3$) δ 1.35 (3H, t, J=7 Hz), 3.90 (3H, s), 4.32 (2H, q, J=7 Hz), 6.02 (2H, s), 7.16 (1H, d, J=1.5 Hz), and 7.29 (1H, d, J=1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.08 (q), 56.33 (q), 60.69 (t), 102.00 (t), 103.52 (d), 109.96 (d), 124.56 (s), 139.19 (s), 143.04 (s), 148.48 (s), and 165.55 (s).

7) cf. Y. Asakawa, R. Matsuda, and A. Cheminat, Phytochemistry, 26, 1117 (1987); T. Matsuoka, S. Imai, T. Yamaguchi, M. Morihira, and M. Murakami, Bull. Chem. Soc. Jpn., 58, 346 (1985).

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