A New Lignan, (-)-Parabenzoinol, from *Parabenzoin trilobum* Nakai

Daisuke Takaoka, Hiroyuki Tani,† and Hiroshi Nozaki††
Department of Chemistry, Faculty of General Education, Ehime University, Matsuyama 790
†Advanced Instrumentation Center for Chemical Analysis, Ehime University, Matsuyama 790
††Department of Biological Chemistry, Faculty of Sciences, Okayama University of Science, Okayama 700

(Received June 16, 1995)

A new tetrahydrofuranol lignan, named (-)-parabenzoinol was isolated from the fresh leaves of *Parabenzoin trilobum* Nakai (Lauraceae), and its structure has been elucidated by X-ray crystallographic analysis. The isomeric properties of the compound in dimethylsulfoxide solution have been studied on the basis of ^{1}H and ^{13}C NMR spectroscopy.

In earlier papers[1-3] we reported the isolation and structure determination of lignans from leaves of genus *Cinnamomum* and *Machilus*, belonging to the family Lauraceae. As a part of our chemical studies on lignans of the family Lauraseae, we have investigated *Parabenzoin trilobum* Nakai which is a deciduous shrub widely distributed over the southern parts of Japan. Although many sesquiterpenoids[4] having insect feeding inhibition as the components of above leaves were already isolated and their structures were determined, only two lignans, (-)-parabenzlactone[5] **1** and acetylparabenzylactone[6] **2**, were so far reported. This paper describes the isolation of a new hemiacetaloid lignan, named parabenzoinol **3** from *Parabenzoin trilob*um Nakai. (Lauraceae) and its structure elucidation performed by X-ray crystallographic analysis. The obtained compound has interesting property that the compound was easily isomerized to **4** by only dissolving in dimethylsulfoxide. The structure of **4** was also elucidated on the basis of ^{1}H and ^{13}C NMR spectroscopic studies.

The acetone extract of fresh leaves was partitioned between ethyl acetate and water. The ethyl acetate soluble portion was subjected to silica gel column chromatography to give the novel lignan parabenzoinol **3** as colorless needles, mp. 191-192 °C together with **1** and **2**. The IR spectrum showed the absorptions due to hydroxyl groups (ν 3360 and 3480 cm^{-1}), an aromatic nucleus (ν 1490, 1510, and 1610 cm^{-1}) and aromatic ether groups (ν 925, 1040, and 1250 cm^{-1}). The HRMS of **3** established the formula as $C_{20}H_{20}O_7$ [found *m/z* 372.1198 (M$^+$), calcd for $C_{20}H_{20}O_7$ (372.1207)]. Proof for the structure of **3** was provided by single-crystal X-ray crystallographic analysis. A crystal of **3** very slowly grown from ethyl acetate at -15 °C was mounted on a four circle automatic Rigaku AFC5R diffractometer to obtain crystal data as follows; $C_{20}H_{20}O_7$, M = 372.37, orthorhombic, $P2_12_12_1$, a = 9.187(7), b = 33.686(9), c = 7.502(4) Å, V = 2322(2) Å^3, D_{calc} = 1.317 gm^{-3}, Z = 4. Of the 1664 reflections collected, 1492 were judged to be observed after normal correction (Cu-$K\alpha$: 1.5418 Å). The crystal structure was solved by direct method using Rigaku TEXSAN program system. Full-matrix least square refinement with anisotropic parameters for the nonhydrogen atoms converged to an R factor of 0.045. The range of standard deviations of bond lengths were 0.005 to 0.009 (Å) and 0.3 to 0.6°, respectively.

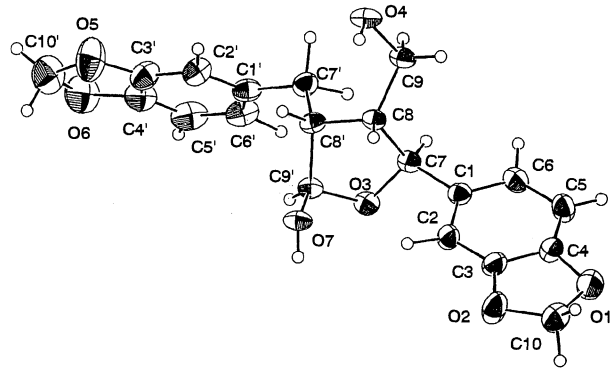
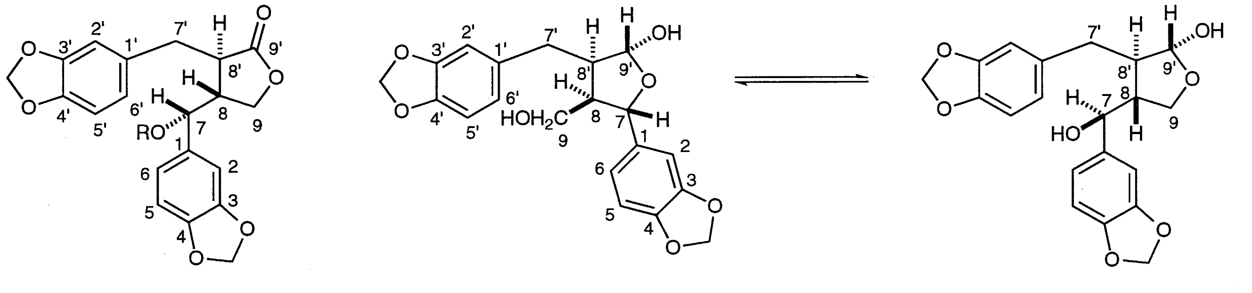


Figure1. Perspective drawing of (-)-parabenzoinol.

The isolated compound showed a single spot by TLC in different solvent systems. However, the ^{1}H and ^{13}C-NMR spectra of **3** measured in a $CDCl_3$ or C_5D_5N solution showed a very complex signals compared with the number of protons and carbons based on the molecular formula, while those of **3** in a dimethylsulfoxide-d$_6$ solution ($[\alpha]_D$ -33° (c 1.4, DMSO-d$_6$)) exhibited significant informations supporting the presence of a single chemical species. The latter spectra showed signals due to two aromatic methylene dioxy groups [δ_H 5.95 and 5.97 (each 2H, s)] and six aromatic protons, appeared between δ_H 6.52 and 6.85 as well as eight aliphatic protons. Detailed assignments of six aromatic protons showed the presence of two sets of 1,2,4-trisubstituted benzene rings [δ_H 6.70 (1H, dd, J=1.5, 7.9 Hz), 6.77 (1H, d, J=1.5 Hz), and 6.79 (1H, d, J=7.9 Hz); δ 6.56 (1H, dd, J=1.5, 7.9 Hz), 6.64 (1H, d, J=1.5 Hz), and 6.75 (1H, d, J=7.9 Hz)]. The ^{13}C-NMR spectrum showed the presence of an oxygen-bearing methylene group [δ_C 67.54 (C-9)], a benzylic methylene group [δ_C 38.57 (C-7')], two methine groups [δ_C 50.88 and 49.99 (C-8, 8')], an oxybenzylic methine group [δ_C 73.61 (C-7)], and a two-oxygens-bearing methine group [δ_C 101.51 (C-9')], respectively. The consecutive losses of two molecules of water [*m/z* 355 (MH$^+$-18), *m/z* 337 (MH$^+$-36)] in its CI-MS suggested that two of remaining oxygen atoms in **3** were present in hydroxyl groups. One of them was a hemiacetal group, which was deduced by the presence of a methine doublet signal at δ_H 4.93 as well as a signal at δ_C 101.51 assignable to carbon attached to two oxygen atom in the ^{13}C-NMR spectrum. The relationships of aliphatic protons were established by ^{1}H-^{1}H COSY spectrum and by EI-MS fragment ion at *m/z* 135 due to benzylic cleavage as its base peak, which would be expected for a 3,4-methylenedioxybenzyl group sited at C-8' [δ_H 2.25 (1H, m)]. The multiplet due to a methine group [δ_H 2.13 (1H,



1: R = H
2: R = Ac

3

4

Scheme 1.

m), H-8] correlated with a pair of double doublets due to oxymethylene [δ_H 3.54 (1H, dd, J=8.2, 7.9 Hz), 3.62 (1H, dd, J=8.2, 8.4 Hz), H-9], a methine [δ_H 2.25 (1H, m), H-8'), and an oxybenzylic methine groups [δ_H 4.48 (1H, br. t, J=6.1 Hz), H-7), and the multiplet due to another methine group (H-8') correlated with a benzylic methylene group [δ_H 2.49 (2H, m), H-7'] and a hemiacetal proton [δ_H 4.93 (1H, d, J=5.2 Hz), H-9']. Furthermore, in the COLOC spectrum, a signal assignable to a benzyl methylene proton at C-7' showed cross peaks with the carbon signals assignable to C-1', C-6', C-2', C-8', and C-9', respectively. Similarly, the proton signals corresponding to oxybenzylic methine at C-7 and hemiacetal methine at C-9' were correlated with the carbon signals assignable to C-2 and C-6, and C-9, respectively.

The above spectral data let us assume that the structure of compound **3** in a DMSO-d_6 solution could have either the 9,9'-monoepoxy or lariciresinol skeleton bearing a hemiacetal group at C-9'. In addition, in the ^{1}H-NMR spectrum (DMSO-d_6, 1.0 wt%, 26.0 C°), two remaining proton signals due to two hydroxyl group protons were observed at δ_H 5.63 (1H, d, J=4.6 Hz) and 5.97 (1H, d, J=5.2) respectively, which were not coupled to the oxygenated methylene but to two oxygenated methine protons. Therefore we proposed for **3** in a DMSO-d_6 solution structure **4** having the secondary hydroxyl group at C-7 and the hemiacetal group at C-9'. The orientation of the hydroxyl group at C-9' was assumed to be α, since a small coupling constant (J < 1) was observed between H-9' and H-8' of **4**.[7] The chemical shifts, narrow benzylic protons at δ_H 2.49 and non-equivalent protons at C-9 supports the *trans* stereochemistry at H-8 and H-8'.[8] In addition, the configuration of a secondary hydroxyl group at C-7 was proposed on the basis of the value of the coupling constant ($J_{7,8}$=6.8 Hz). This implied a predominantly *anti* conformation for these two protons. Its stereochemistry was also supported by the fact that the configurations of C-8, C-8', and C-7 obtained from an X-ray structure determination of compound **3** are generally held in the course of the transhemiacetalization.

In conclusion, the compound **3** has the unique property to be isomerized easily to **4** by merely dissolving in dimethylsulfoxide.

References

1 D. Takaoka, N. Takamatsu, Y. Saheki, K. Kono, C. Nakaoka, and M. Hiroi, *Nippon Kagaku Kaishi*, **1975**, 2197.
2 D. Takaoka, K. Watanabe, and M. Hiroi, *Bull. Chem. Soc. Jpn.*, **49**, 3564 (1976).
3 D. Takaoka, M. Imooka, and M. Hiroi, *Bull. Chem. Soc. Jpn.*, **50**, 2821 (1977).
4 K. Wada, Y. Enomoto, and K. Munakata, *Agric. Biol. Chem.*, **34**, 946 (1970).
5 K. Wada and K. Munakata, *Tetrahedron Lett.*, **23**, 2017 (1970).
6 M. Niwa, M. Iguchi, S. Yamamura, and S. Nishibe, *Bull. Chem. Soc. Jpn.*, **49**, 3359 (1976).
7 R. C. Cambie, G. R. Clark, P. A. Craw, T. C. Jones, P. S. Rutledge, and P. D. Woodgate, *Aust. J. Chem.*, **38**, 1631 (1985).
8 J. E. T. Corrie, G. H. Green, E. Ritchie, and W. C. Taylor, *Aust. J. Chem*, **23**, 133 (1970).