BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 49 (11), 3359—3360 (1976)

The Stereostructure of Acetylparabenzlactone and Its Conversion to a Lariciresinol-type Lactone

Masatake NIWA, Masanobu IGUCHI, Shosuke YAMAMURA, and Sansei NISHIBE*

Faculty of Pharmacy, Meijo University, Tenpaku-ku, Nagoya 468
**Faculty of Pharmacy, Higashi Nippon Gakuen University, Ishikari-gun, Hokkaido 061-02*

(Received June 15, 1976)

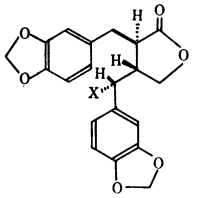
Synopsis. Acetylparabenzlactone (**1**), an acetylation product of (−)-parabenzlactone (**2**), has been newly isolated from *Parabenzoin trilobum* Nakai, and the stereostructures of these two piperolignanolides have also been elucidated. Furthermore, the chemical conversion of **1** to a lariciresinol-type lactone (**3**) has been carried out.

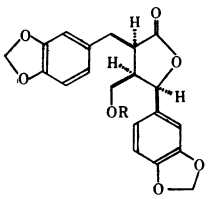
In the course of our search for such an epoxygermacrene as shiromodiol,[1] which has been used for a biogenetic-type reaction,[2] we have isolated a new lignanolide, named acetylparabenzlactone (**1**), from *Parabenzoin trilobum* Nakai instead of (−)-parabenzlactone (**2**),[3] whose stereostructure remains unsettled.

Fresh leaves of the same plant[4] were extracted with hot benzene. The benzene extract was repeatedly chromatographed on silica gel, and then purified by preparative TLC to give colorless needles of acetylparabenzlactone (**1**) in a 0.017% yield.

The UV and NMR spectra of **1** indicate the presence of two methylenedioxyphenyl groups [δ 5.91 (2H, s), 5.92 (2H, s) and 6.60 (6H, complex)]. Furthermore, this lignanolide is proved to have a five-membered ring lactone and a secondary acetoxyl group [δ 2.10 (3H, s) and 5.70 (1H, d, J=6.0 Hz)]. From these data, this lignanolide (**1**) must be regarded as an acetylation product of (−)-parabenzlactone (**2**), which has previously been reported by Wada and Munakata.[3] Thus, the former was readily converted to **2** on treatment with 2% methanolic KOH (room temp, 1.5 h), giving a mixture of two hydroxyl lactones (**2** and **3**) with the same molecular formula ($C_{20}H_{18}O_7$) in 65 and 21% yields respectively. One of them is completely identical with an authentic sample of (−)-parabenzlactone (**2**) (mixed mp and IR spectrum). The structure of isoparabenzlactone (**3**) was also established (see below). In addition to the two original methylenedioxyphenyl groups, this compound has a five-membered ring lactone grouping [ν_{max} 1770 cm^{-1}; δ 5.13 (1H, d, J=8.0 Hz)]. In particular, the presence of a hydroxymethyl group in **3** can be confirmed by its NMR spectrum, which has a signal at δ 3.50 (2H, complex) which is shifted to δ 3.95 on acetylation, giving the corresponding acetate (**4**). From these data, isoparabenzlactone should be a lariciresinol-type lactone (**3**), whose stereostructure is based on those of **1** and **2**.

On hydrogenolysis over a freshly prepared palladium catalyst in EtOH containing $HClO_4$, (−)-parabenzlactone (**2**) was readily converted to (−)-hinokinin (**5**) in a 71% yield (IR and CD spectra).[5] Finally, the configuration of the remaining OH group in **2** is based on the NMR signal at δ 4.60 assignable to the proton attached to the carbon atom bearing the OH group, whose coupling constant is 6.5 Hz,[6] indicating that (−)-parabenzlactone adopts the stereostructure depicted in **2**. Thus, acetylparabenzlactone also has the **1** stereostructure.





1 X=OAc
2 X=OH
5 X=H

3 X=H
4 X=Ac

Experimental

All the mps are uncorrected. The IR spectra were recorded on a Hitachi-215 spectrophotometer. The UV spectra were taken on a Hitachi-124 spectrophotometer, using MeOH as the solvent. The NMR spectra were recorded on a JEOL JNM-PS 100 NMR spectrometer, using $CDCl_3$, unless otherwise stated. The chemical shifts are given in ppm relative to the internal TMS; only prominent signals are cited (d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet). The mass spectra were obtained on a Hitachi RMU-6D mass spectrometer, operating with an ionization energy of 70 eV. The optical rotation was measured on a JASCO Model DIP-SL automatic polarimeter.

Isolation of Acetylparabenzlactone (1). Fresh leaves of *Parabenzoin trilobum* Nakai (15 kg) immersed in benzene (100 l) were heated under reflux for 7 h and then filtered. The filtrates were concentrated under reduced pressure to obtain a viscous residue. After the above procedure has been repeated, the total weight of the benzene extracts thus far obtained was 430 g. The viscous residue (100 g) was chromatographed on silica gel (Mallinckrodt, 100 mesh) (900 g). After the elution of shiromodiol monoacetate[1] with hexane–AcOEt (3: 1), further elution with hexane–AcOEt (2: 1) afforded a crude oil (3.0 g), which was then rechromatographed on silica gel (Mallinckrodt, 100 mesh) (55 g) and eluted with $CHCl_3$ to give a slightly crude material (1.5 g). Further purification was carried out using preparative TLC (Kieselgel PF_{254}; $CHCl_3$) to give colorless needles of acetylparabenzlactone (**1**) (605 mg) in a pure state; mp 134—136 °C (from hexane–benzene)[7]; $[\alpha]_D^{28}$ −19.6° (c=0.82 in dioxane); λ_{max} 286 and 236 nm (ε, 7500 and 7800 respectively); ν_{max} ($CHCl_3$) 1770, 1745, 1240, and 1045 cm^{-1}; δ 2.10 (3H, s), 2.6—3.0 (4H, complex), 3.94 (2H, complex), 5.70 (1H, d, J=6.0 Hz), 5.91 (2H, s), 5.92 (2H, s), and 6.60 (6H, complex); m/e 412 (M^+), 352, 175, 151, and 135 (Found: C, 64.24; H, 4.80%. Calcd for $C_{22}H_{20}O_8$: C, 64.07; H, 4.89%).

Base-catalysed Reaction of Acetylparabenzlactone (1). A solution of **1** (150 mg) in 2% methanolic KOH (10 ml) was stirred at room temperature for 1.5 h, and then made acidic

with a dil HCl aq solution and extracted with $CHCl_3$. The extract was washed with water and then dried over anhydrous $MgSO_4$. The subsequent removal of the solvent under reduced pressure gave a pale yellow liquid, which was separated by preparative TLC (Kieselgel PF_{254}) using $CHCl_3$–Et_2O (3: 1) to give two deacetyl compounds [**2** (88 mg) and **3** (28 mg)] in a pure state. The physical data of these two compounds are shown below. Particularly, the recrystallization of the former from hexane–benzene gave (−)-parabenzlactone (**2**) with a mp of 156—158 °C (lit,[3] 159—161 °C) (mixed mp and IR spectrum); δ 1.64 (1H, br. s), 2.13 (1H, br. s, OH), 2.60 (1H, q, J=7.5 Hz), 2.95 (2H, br. s), 3.94 (2H, d, J=7.0 Hz), 4.60 (1H, d, J=6.5 Hz), 5.92 (2H, s), 5.96 (2H, s), and 6.68 (6H, complex); *m/e* 370 (M^+), 352, 175, 151, and 135 (Found: C, 65.04; H, 4.68%. Calcd for $C_{20}H_{18}O_7$: C, 64.86; H, 4.90%).

*Isoparabenzlactone (**3**) as a Colorless Viscous Liquid*: ν_{max} ($CHCl_3$) 3400 and 1770 cm^{-1}; δ 1.92 (1H, s, OH), 2.25 (1H, br. s), 3.03 (3H, complex), 3.50 (2H, complex), 5.13 (1H, d, J=8.0 Hz), 5.92 (2H, s), 5.93 (2H, s), 6.59 (1H, s), and 6.70 (5H, near s); *m/e* 370 (M^+), 178, 151, and 135 (Found: *m/e* 370.10706. Calcd for $C_{20}H_{18}O_7$: *m/e* 370.10523).

*Acetylation of (−)-Parabenzlactone (**2**).* A solution of **3** (35 mg) in Ac_2O–pyridine [1: 2 (1.5 ml)] was allowed to stand at room temperature overnight and was then diluted with $CHCl_3$ (30 ml). The chloroform solution was washed with water and then dried over anhydrous $MgSO_4$. The subsequent removal of the solvent under reduced pressure left a residue which was purified by preparative TLC (Kieselgel PF_{254}; $CHCl_3$) to give the original acetate (**1**) (33 mg) (mp, TLC and IR spectrum).[3,7]

*Acetylation of Isoparabenzlactone (**3**).* According to the same procedure as has been described above, the alcohol **3** (30 mg) was treated with Ac_2O–pyridine [1: 2 (1.5 ml)] to give a colorless viscous liquid (27 mg), which was then crystallized from hexane–benzene to afford colorless needles of acetylisoparabenzlactone (**4**); mp 56—58 °C; $[\alpha]_D^{28}$ +97.3° (*c* 1.47 in dioxane); λ_{max} 287 and 237 nm (ε, 7300 and 7700, respectively); ν_{max} ($CHCl_3$) 1770 and 1740 cm^{-1}; δ 2.00 (3H, s), 2.43 (1H, heptette, J=8.0 Hz), 2.8—3.2 (3H, complex), 3.95 (2H, m), 4.98 (1H, d, J=8.5 Hz), 5.91 (2H, s), 5.92 (2H, s), and 6.70 (6H, complex); *m/e* 412 (M^+), 220 and 135 (Found: *m/e* 412.11389. Calcd for $C_{22}H_{20}O_8$: *m/e* 412.11581).

*Hydrogenolysis of (−)-Parabenzlactone (**2**).* The catalytic hydrogenation of **2** (15 mg) in EtOH (3 ml) containing 3 drops of a 60% aq. $HClO_4$ solution was carried out over freshly prepared palladium (30 mg) at room temperature overnight. After the addition of AcOEt (20 ml), the catalyst was removed by filtration. The filtrate was washed with water and then dried over anhydrous $MgSO_4$. The subsequent removal of the solvent under reduced pressure gave a crude oil, which was purified by preparative TLC (Kieselgel PF_{254}; $CHCl_3$) to give a colorless viscous liquid (10 mg) which was completely identical with an authentic sample of (−)-hinokinin (**5**) (IR and CD spectra).

The authors wish to thank Professor Katsura Munakata and Dr. Kojiro Wada (Nagoya University) for providing them with the authentic samples of (−)-parabenzlactone and its acetate. They are also indebted to Professor Masao Noro (Meijo University) for the collection of the plant *Parabenzoin trilobum* Nakai.

References

1) K. Wada, K. Matsui, Y. Enomoto, O. Ogiso, and K. Munakata, *Agr. Biol. Chem.*, **34**, 941 (1970); K. Wada, Y. Enomoto, and K. Munakata, *ibid.*, **34**, 946 (1970).

2) M. Niwa, M. Iguchi, and S. Yamamura, *Tetrahedron Lett.*, **1975**, 3661.

3) K. Wada and K. Munakata, *Tetrahedron Lett.*, **1970**, 2017.

4) Collected at Sanage, Aichi-ken, in late October.

5) R. S. Burden, L. Crombie, and D. A. Whiting, *J. Chem. Soc., C*, **1969**, 693, and the references cited therein.

6) M. Kuhn and A. von Wartburg, *Helv. Chim. Acta*, **50**, 1546 (1967).

7) Wada and Munakata have reported that an acetylation product of (−)-parabenzlactone has a melting point (142—146 °C) different from ours. This is due to the use of different kinds of recrystallization solvents.