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Synthesis of 7-Desoxypanepoxydol[1]

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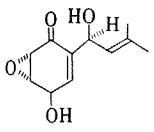
7-Desoxypanepoxydol is one of the metabolties isolated from culture broth of *Panus rudis* with other metabolites, antitumor panepoxydon[1] (**1**) and panepoxydion[2] (**2**). As a part of the synthetic studies



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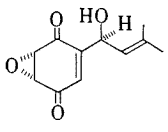

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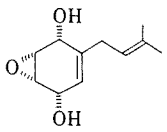

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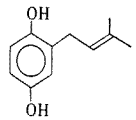
of highly oxygenated cyclohexane derivatives,[3] this paper describes the synthesis of 7-desoxypanepoxydol (**3**).



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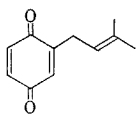

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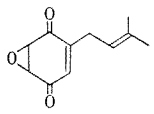

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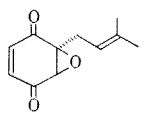

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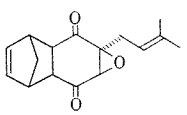

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O-Isopentenyl hydroquinone (**4**) was prepared from hydroquinone and 2-methylbut-3-en-2-ol according to modified procedure of L. Jurd *et al.*[4] Oxidation of I with lead tetraacetate in acetic acid or ferric chloride in methanol gave 2-isopentenyl-1,4-benzoquinone,[5] mp 30°C, in high yield. Epoxidation of the benzoquinone with sodium perborate in tetrahydrofuran at pH 8.5 afforded a mixture consisting of two epoxides, 7-desoxypanepoxydion (**6**) and iso-7-desoxypanepoxydion (**7**), whose presence were confirmed by NMR spectrum in which a signal at δ 6.35 (a vinylic proton) and a signal at δ 6.60 (two vinylic protons) come of epoxides **6** and **7** respectively. Since direct separation of the mixture by chromatography was difficult and only a part of the mixture was separated to give pure 7-desoxypanepoxydion (**6**) which was identified by the comparison with spectral data of authentic sample derived from natural 7-desoxypanepoxydol (**3**). Therefore, the mixture was treated with cyclopentadiene and the reaction mixture effectively separated to give 7-desoxypanepoxydion (**6**) and Diels-Alder **8**, mp 65°C.[5]

Reduction of **6** with zinc borohydride in ether[6] afforded products, one of which showed the same *Rf* value with natural 7-desoxypanepoxydol (**3**) and separated by chromatography with other product. The synthetic 7-desoxypanepoxydol (**3**) was identical with natural sample in IR spectrum.

EXPERIMENTAL

IR spectra were obtained with a Hitachi EPI-S2 spectrometer. PMR spectra were recorded on a Hitachi R-22 and a JASCO PS-100 High Resolution NMR spectrometer. Chemical shifts are expressed in δ value.

o-Isopentenyl hydroquinone (**4**)

o-Isopentenyl hydroquinone was prepared according to modified procedure of Jurd *et al.*[4] A solution of 22 g of hydroquinone in 35 ml of hot water and 15 ml of formic acid at 80°C was cooled to 60°C and 15 g of 2-methylbut-3-en-2-ol was added dropwise to the solution under stirring. The reaction mixture was allowed to stand overnight. The precipitated crystals were collected and the dried crystals were chromatographed on 50 g of silicic acid. The column was eluted with chloroform-methanol (9: 1) to give 6 g of *o*-isopentenyl hydroquinone (**4**), mp 102°C and 2.6 g of diprenylhydroquinone, mp 148°C.

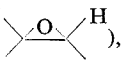
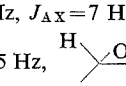
2-Isopentenyl-1,4-benzoquinone (**5**)

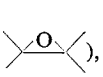
a) *Oxidation by lead tetraacetate.* To a solution of 3 g of *o*-isopentenyl hydroquinone (**4**) in 145 ml of acetic acid was added a solution of 14.5 g of lead tetraacetate in 400 ml of acetic acid. After 30 min the reaction mixture was concentrated and the residue was extracted with chloroform and the extracts were dried over anhydrous sodium sulfate. The extracts were evaporated *in vacuo* to give 2.7 g of yellow needles (**5**), mp 30°C.

b) *Oxidation by ferric chloride.* To a solution of 4.7 g of *o*-isopentenyl hydroquinone (**4**) in 100 ml of methanol was added a solution of 15 g of ferric chloride in 50 ml of water. The reaction mixture was allowed to stand for 2 hr at room temperature and extracted with chloroform. The extracts were dried over anhydrous sodium sulfate and evaporated *in vacuo* to give 4.0 g of the benzoquinone (**5**).

7-Desoxypanepoxydion (**6**) *and iso-7-desoxypanepoxydion* (**7**)

A solution of 18 g of sodium perborate in 900 ml of water was adjusted at pH 8.5 with acetic acid and the solution was added to a solution of 4.6 g of the

benzoquinone in 300 ml of tetrahydrofuran and the extracts were dried over anhydrous sodium sulfate and evaporated *in vacuo* to give a residue. The residue was chromatographed on silicic acid to give 7-desoxypanepoxydion (**6**), IR ν_{max}^{film} cm^{-1} 1685, 1615, *m/e*: 192 (M^+), PMR (δ in $CDCl_3$) 1.60, 1.75 (each 3H, s, $=C(CH_3)_2$), 3.00 (2H, d, J=7.0 Hz, -CH-), 3.80 (2H, m, ), 5.10 (1H, t, J=7 Hz, ), 6.35 (1H, m, $=CH$) and iso-7-desoxypanepoxydion, IR ν_{max}^{film} cm^{-1} 1690, PMR (δ in $CDCl_3$) 1.65, 1.73 (each 3H, $=C(CH_3)_2$), 2.40, 3.00 (2H, AB part of ABX spin system, J_{AB}=15 Hz, J_{AX}=7 Hz, J_{BX}=8 Hz, $-CH_2-$), 3.65 (1H, d, J=1.5 Hz, ), 5.10 (1H, q, X part of ABX spin system, J_{AX}=7 Hz, J_{BX}=8 Hz, ) 6.60 (2H, broad s, ).

Effective separation of **6** and **7** was carried out as follows. To a solution of 3.4 g of the extracts in 15 ml of tetrahydrofuran was added 1 g of cyclopentadiene and the reaction mixture was allowed to stand for 1 day and concentrated *in vacuo* to give a residue. The residue was chromatographed on silicic acid to give 2 g of 7-desoxypanepoxydion and 1 g of 2-isopentenyl-5,8-methano-4a,5,8,8a-tetrahydro-1,4-naphthoquinone-2,3-epoxide (**8**). IR ν_{max}^{KBr} cm^{-1} 1700, PMR (δ in $CDCl_3$) 1.20~1.50 (2H, m, $-CH_2-$), 1.52, 1.62 (each 3H, s, $=C(CH_3)_2$), 2.54 (2H, d, J=7 Hz, $-CH_2-$), 3.30 (2H, m, $-CH(-C(=O)-)-$), 3.35 (1H, s, ), 3.48 (2H, m, $C(-C-)-$),5.00 (1H, t, J=7 Hz), 6.00 (2H, m, ), mp 64.0~64.8°C. *Anal.* Calcd. for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.42; H, 6.94.

7-Desoxypanepoxydol. A solution of 500 mg of 7-desoxypanepoxydion in 10 ml of anhydrous ether was added to a solution of 10 ml of zinc borohydride prepared according to the procedure of Gensler *et al.*[6] The reaction mixture was stirred for 20 min and to the mixture was added water and the mixture was extracted with ethyl acetate. The extracts were dried on anhydrous sodium sulfate and evaporated *in vacuo* to give a residue. The residue was chromatographed twice on silicic acid and the column was eluted with ethyl acetate-petroleum ether (4:3) to give 15 mg crystalline compound which has the same *Rf* value with natural sample **3**, mp 95~98°C. *m/e* 196 (M^+), IR ν_{max}^{Nujol} cm^{-1} 3320, 3250, 1240, 1130, 890, 850. PMR (δ in $(CD_3)_2SO$), 1.62, 1.72 (each 3H, s, $=C(CH_3)_2$), 2.75 (2H, d, J=7 Hz $-CH_2-$), 3.25, 3.35 (each 1H, m,), 4.15, 4.25 (each 1H, m, -CHOH), 5.00, 5.15 (each 1H, m, OH), 5.10, 5.25 (each 1H, m, $=CH_2$).

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4) L. Jurd, K. Steven and G. Manners, *Tetrahedron Letters*, **1971**, 2275.
5) The same kind of treatment was carried out in the synthesis of phyllostine see Ref. 3a and 3c.
6) W. J. Gensler, F. Johnson and A. D. B. Sloan, *J. Am. Chem. Soc.*, **82**, 6074 (1960).