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LACTONES OF SAKHALIN CORK TREE

PHELLODENDRON SACCHALINENSE (FR. SCHMIDT) SARG.

(Presented by Academician A. I. Oparin, 16 X 1962)

Sakhalin cork tree is a deciduous tree 15-20 m high, of the family Rutaceae, growing on southern Sakhalin, the Kuril Islands, in Korea, and in northern Japan; it is cultivated as an ornamental in Europe and North America ([1]). The roots and bark of the plant are used in the medicine of China and Japan as a medicinal remedy ([2],[3]). Chemically it has been little studied: the alkaloids berberine and phellodendrine have been isolated from the roots. From a closely related species, Amur cork tree (*Phellodendron amurense* Rupr.), the alkaloids berberine, palmatine, magnoflorine, phellodendrine, candicine, jatrorrhizine, coptisine, worenine, guanidine, and an unknown base with m.p. of the picrate 230° ([4-9]) have been isolated, as well as nitrogen-free substances –the ketone obakunone $C_{27}H_{33}O_7$ + $6H_2O$ or $C_{28}H_{35}O_7$ + $6H_2O$, obakulactone (limonin) $C_{26}H_{30}O_8$, phytosterol $C_{26}H_{44}O$, palmitic and linoleic acids ([10-14]), the flavonoids phellamurin $C_{26}H_{32}O_{12}$ and amurensin $C_{26}H_{30}O_{12}$, and lumiceruleic acid ([15]). Proceeding from the phylogenetic closeness of the named species and the valuable medicinal properties of Sakhalin cork tree, its chemical study was of interest. The object of investigation was the bark of the plant, collected in the Far East by an expedition of the All-Union Scientific Research Institute of Medicinal and Aromatic Plants (A. I. Shreter).

Preliminary investigations established that the bark contained 1.10% lactones, during the study of which two crystalline substances were isolated–$C_{25}H_{30}O_7$ (A) and $C_{26}H_{30}O_8$ (B). Isolation of substance A was carried out by the following procedure. The comminuted bark of *Phellodendron sacchalinense* was extracted twice with strong alcohol, then with alcohol containing 2% HCl. The extracts were combined, concentrated in vacuo to a thick syrup, and left at room temperature. The separated yellow-brown crystalline precipitate (6.92%) was filtered off, washed with ether, and repeatedly extracted with hot water. On cooling of the aqueous extracts, a yellow crystalline substance separated, with m.p. 189° (decomposition), giving reactions for alkaloids and identified by

the mixed tartrate test (m.p. 198°) with berberine. The yield of the latter was 1.01%.

The residue after extraction with water (1.23%) was repeatedly recrystallized from 70° alcohol. This gave a colorless crystalline substance with m.p. 224° (corrected), $[\alpha]_D^{25} - 80.8^\circ$ (acetone, $C = 1.36$).

Found, %: C 67.54, 67.81; H 6.74, 6.85; H (mobile) 0.17, 0.18
$C_{25}H_{30}O_7$. Calculated, %: C 67.87; H 6.78; H (mobile) 0.22

Molecular weight by Rast found 462, calculated 442.

The substance dissolved well in chloroform, acetone, and dioxane, less readily in hot alcohol and ether, and did not dissolve in water. The alcoholic solutions had a neutral reaction, reduced Fehling' s solution on heating, but did not react with ammoniacal silver solution and fuchsin-sulfurous acid, decolorized solutions of bromine in carbon tetrachloride and potassium permanganate, and did not give a reaction with diazo-

with titrated sulfanilic acid solution and ferric chloride. The substance had the properties of a lactone—it did not react with solutions of caustic alkalis in the cold, but on heating gave colorless solutions. Determination of the gram-equivalent by titration showed that the latter was half the molecular weight.

By known methods, the 2,4-dinitrophenylhydrazone with m.p. 289° (corrected) and the semicarbazone with m.p. 259° (corrected) were obtained.

2,4-Dinitrophenylhydrazone:

Found %:	C 60.10, 60.19;	H 5.74, 5.68;	N 9.12, 8.79
Calculated %:	C 59.61;	H 5.77;	N 8.96

The IR spectrum of the substance showed the presence of absorption maxima λ_{max} 1707 cm^{-1} (ketones) and 1747 cm^{-1} (δ-lactones). In the absence of hydroxy and carboxy groups (according to the IR spectrum and acylation and methylation experiments), the substance contained labile hydrogen.

On the basis of the physicochemical properties given above, it may be concluded that substance A is a keto-δ-dilactone, and its expanded formula may be represented as follows: $C_{22}H_{30}O_2(CO)(COO)_2$. In composition and properties it is a new lactone, not described in the literature, and we have named it phellandron.

On acidification of alkaline solutions of phellandron, a colorless crystalline substance with m.p. 204° (from methanol) was obtained. In its IR spectrum the following maxima were noted: 1756 cm^{-1} (δ-lactone), 1711 cm^{-1} (keto group), 2705, 2548, and 1629 cm^{-1} (acids), and 3360 cm^{-1} (hydroxyl). The presence of hydroxy and carboxy groups was confirmed by determining an additional two atoms of labile hydrogen (on heating).

Found %: H (labile) 0.63
Calculated %: 3H 0.66

In this connection, it may be assumed that the substance obtained was a ketooxy acid with one lactone ring, formed as a result of lactonization of only one pair of hydroxyl and carboxyl groups.

Substance B was isolated by us from the mother liquor after separation of berberine and phellandron. For this purpose the mother liquor was diluted with water 1:1 and extracted repeatedly with ether. The ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated to a small volume. The precipitate that separated in this process (0.11%) was filtered off and recrystallized from acetone, then from methanol. A colorless crystalline substance was obtained with m.p. 280–281° (corrected), $[\alpha]_D^{25} - 34.08^\circ$ (acetone, C 2.61) and $+31.91^\circ$ (0.5 N KOH solution), readily soluble in acetone and ethyl acetate and insoluble in water.

$C_{26}H_{30}O_8$. Found %: C 66.61, 66.31; H 6.56, 6.35; H (labile) 0.24, 0.23
Calculated %: C 66.38; H 6.38; 1H (labile) 0.21

Molecular weight by Rast found 508, calculated 470.

The substance was neutral in character and had the properties of a lactone. Its aqueous-alcoholic solutions did not reduce Fehling' s solution and did not decolorize solutions of bromine and potassium permanganate. The reaction with diazotized *p*-nitroaniline and ferric chloride was negative. The gram-equivalent of the substance was half the molecular weight. The IR spectrum showed the presence of a maximum at 1741 cm^{-1}, corresponding to a δ-lactone. In the absence of hydroxy and carboxy groups, the presence of one atom of labile hydrogen was established. In composition and melting point, substance B resembles the dilactone limonin, previously isolated from a number of plants [16–22]. At the same time, a difference is observed in optical activity, which in alkaline medium is the same for these substances, but in acetone has

different values. A difference was also noted when comparing the IR spectra. These data allow the isolated substance to be regarded as a new dilactone, which we have named phellandrin.

Upon acidification of alkaline solutions of phellandrin, a crystalline substance with m.p. 277° (from methanol) was obtained, poorly soluble in ether and insoluble in water. Its IR spectrum showed maxima at λ_{max} 1745 cm^{-1} (δ-lactone), 3662 and 3336 cm^{-1} (hydroxyl), 2685, 2605, 1671, and 1638 cm^{-1} (carboxyl). Thus, in the nature of its interaction with alkali and the closure of the lactone ring, phellandrin resembles phellandron.

Thus, from the bark of Sakhalin cork tree, two new lactones have been isolated and characterized: the keto-δ-dilactone $C_{25}H_{30}O_7$ and the δ-dilactone $C_{26}H_{30}O_8$, named respectively phellandron and phellandrin.

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Note: Figure translations are in progress. See original paper for figures.