429. 2:4:3':5'-Tetrahydroxystilbene from Artocarpus lakoocha. By S. Mongolsuk, Alexander Robertson, and R. Towers.

A polyhydric phenol from Artocarpus lakoocha has been shown to be 2:4:3':5'-tetrahydroxystilbene.

CONCENTRATION of a hot aqueous extract of the powdered wood of the Siamese tree Artocarpus lakoocha gave a phenolic product from which a tetrahydric phenol with strong reducing properties was isolated as a dihydrate of empirical formula $C_{14}H_{12}O_4, 2H_2O$, m. p. 201°, devoid of C-methyl or methoxyl group. This unsaturated compound, which formed a tetra-acetate, a tetrabenzoate, and a tetramethyl ether, was shown to contain one ethylene group by perbenzoic acid titration and on hydrogenation furnished a saturated dihydro-derivative which gave a tetra-acetate and a tetramethyl ether. On oxidation with potassium permanganate the tetramethyl ether of the parent phenol yielded a mixture of 2:4- and 3:5-dimethoxybenzoic acid whilst ozonolysis of the ether produced a mixture of the corresponding aldehydes, separated as their 2:4-dinitrophenyl-hydrazones.

From these results it seemed clear that the compound was 2:4:3':5'-tetrahydroxystilbene (I) and the synthesis of compound (II), identical with the dihydro-derivative of



the stilbene tetramethyl ether, confirmed this. 2:4:3':5'-Tetrahydroxystilbene has been isolated from the roots of *Neratrum grandiflorum Loes. fil.* by Takaoka¹ who, although he advanced the correct formulation, unfortunately named the stilbene hydroxyresveratrol in spite of the fact that it was devoid of methoxy-group; we consider that this trivial name for the parent stilbene should be abandoned. The annexed Table confirms the identity of the

¹ Takaoka, J. Chem. Soc. Japan, 1939, 61, 96; J. Fac. Sci., Hokkaido Imp. Univ., 1940, III, 3, 1.

products from the two sources. Since our work was completed, Barnes and Gerber² have reported isolation of the stilbene from *Toxylum pomiferum* wood.

	Takaoka's compound	Phenol from Artocarpus lakoocha
Cryst. form		Plates
М. р	199·5°	201°
Ammoniacal AgNO ₃	Reduces	Reduces
Fehling's soln.	Reduces	Reduces
Tetra-acetate	M. p. 142°	M. p. 142°
Tetra-benzoate	M. p. 193.5°	M. p. 193°
Me ₄ ether	Oil	M. p. 84°

EXPERIMENTAL

2:4:3':5'-Tetrahydroxystilbene.—Obtained by concentrating a hot aqueous extract of the powdered wood of Artocarpus lakoocha, the light brown powder contained small amounts of resin and gum. The ethereal extract of the crude product was treated with charcoal and evaporated, leaving a brown syrup which slowly crystallised and then on repeated crystallisation from hot water gave the dihydrate of the tetrahydroxystilbene in plates with a transient blue-green ferric reaction in alcohol, m. p. 201°, after softening at about 150° (depending on rate of heating) (Found, in a dried material: C, $60\cdot2$; H, $5\cdot9$; H₂O, by drying *in vacuo* at 100° , $12\cdot5$. Calc. for C₁₄H₁₂O₄·2H₂O: C, $59\cdot9$; H, $5\cdot8$; H₂O, $12\cdot8$. Found, in anhyd. compound, m. p. 201° without previous softening: C, $69\cdot2$; H, $5\cdot2$. Calc. for C₁₄H₁₂O₄: C, $68\cdot8$; H, $5\cdot0\%$).

The compound, which readily reduced Fehling's solution and ammoniacal silver nitrate, gave, by the methyl sulphate-potassium carbonate method, a tetramethyl ether forming needles, m. p. 84°, from a little methanol, readily soluble in alcohol or benzene and insoluble in aqueous sodium hydroxide [Found : C, 71.9; H, 6.7; OMe, 39.3%; M (Rast), 297. $C_{14}H_8(OMe)_4$ requires C, 72.0; H, 6.7; OMe, 41.3%; M, 300]. Prepared by the pyridine- or sodium acetate-acetic anhydride method, the tetra-acetate separated from alcohol in stout needles, m. p. 142° (Found : C, 63.9; H, 4.9; Ac, 40.4. Calc for $C_{14}H_8O_4Ac_4$: C, 64.1; H, 4.9; Ac, 41.8%). With benzoyl chloride and pyridine the phenol gave the tetrabenzoate, prisms, m. p. 193°, from benzene-light petroleum (b. p. 60-80°) and then aqueous acetic acid (Found : C, 75.8; H, 4.2. Calc. for $C_{24}H_{28}O_8$: C, 76.4; H, 4.2%).

Oxidation of 2:4:3':5'-Tetramethoxystilbene.—(a) Powdered potassium permanganate (2.0 g.) was added in small portions to an agitated solution of the ether (1 g.) in acetone (100 ml.) and water (5 ml.) and after being kept for 1 hr. the mixture was clarified with sulphur dioxide, acidified with a little dilute sulphuric acid, and concentrated *in vacuo*. After isolation the semisolid was extracted with aqueous sodium hydrogen carbonate, the extract was acidified, and the solid, m. p. 160—177°, was repeatedly crystallised from hot aqueous methanol, giving O-dimethyl- α -resorcylic acid, plates, m. p. and mixed m. p. 182° [Found : C, 59·8; H, 5·5; OMe, 34·4. Calc. for $C_7H_4O_2(OMe)_2: C, 59·3; H, 5·5; OMe, 34·0\%$]. Evaporation of the aqueous-methanolic mother-liquors followed by extraction with ether gave 2: 4-dimethoxy-benzoic acid, needles, m. p. and mixed m. p. 109°, from dilute methanol and then light petroleum (b. p. 80—100°) (Found : C, 59·8; H, 5·4. Calc. for $C_9H_{10}O_4: C, 59·3; H, 5·5\%$).

(b) The ozonide from the stilbene tetramethyl ether was decomposed with water, and the product treated with an excess of aqueous 2: 4-dinitrophenylhydrazine sulphate. The resulting mixture of hydrazones, m. p. 240—248°, which could not be satisfactorily resolved by chromatography on aluminium oxide, was separated by fractionation from warm alcohol. The less soluble product was the 2: 4-dinitrophenylhydrazone of 3: 5-dimethoxybenzaldehyde, orange yellow needles, m. p. and mixed m. p. 260—261° (Found: N, 16·2. Calc. for $C_{15}H_{14}O_8N_4$: N, 16·2%). The more soluble fraction consisted of the 2: 4-dinitrophenylhydrazone of 2: 4-dimethoxybenzaldehyde, scarlet needles, m. p. and mixed m. p. 258° (Found: N, 15·6%).

1-(2: 4-Dihydroxyphenyl)-2-(3: 5-dihydroxyphenyl)ethane.—(a) Hydrogenation of 2: 4: 3': 5'tetrahydroxystilbene (1 g.) in methanol (100 ml.) with hydrogen and palladium-charcoal gave the diphenylethane which separated from water as a dihydrate in rectangular plates, m. p. 94—96° (rapid heating) (Found: C, 59·4; H, 6·3; H₂O, 11·5. C₁₄H₁₄O₄,2H₂O requires C, 59·6; H, 6·4; H₂O, 12·8%). On further heating, the compound solidified and then melted at 160°; anhydrous material, m. p. 160°, was also obtained by heating the hydrate *in vacuo* at 80° (Found: C, 68·3; H, 5·8. Calc. for C₁₄H₁₄O₄: C, 68·3; H, 5·7%).

^a Barnes and Gerber, J. Amer. Chem. Soc., 1955, 77, 3259.

This compound gave a negative ferric reaction in alcohol and a blue reaction in water. Prepared by methyl sulphate-potassium carbonate method, the *tetramethyl ether* separated from 95% methanol (charcoal) in needles, m. p. 51-52° [Found : C, 71.4; H, 7.0; OMe, 40.6. $C_{14}H_{10}(OMe)_4$ requires C, 71.5; H, 7.5; OMe, 41.0%]. The *tetra-acetate* formed needles, m. p. 75°, identical with a specimen obtained by the hydrogenation of 2:4:3':5'-tetra-acetoxy-stilbene (Found : C, 64.2; H, 5.3. $C_{22}H_{22}O_8$ requires C, 63.8; H, 5.4%).

(b) 3: 5-Dimethoxybenzyl cyanide (1.75 g.) was condensed with resorcinol (1.1 g.) in ether (75 ml.) by zinc chloride (1 g.) and an excess of hydrogen chloride, and the ketimine washed with much ether and hydrolysed with hot water. A solution of the resulting oil in ether (150 ml.) was washed with aqueous sodium hydrogen carbonate (10 ml. \times 3) to remove traces of acidic material and then extracted with 2% aqueous sodium hydroxide. Acidification of the extracts gave ω -(3: 5-dimethoxyphenyl)resacetophenone, which separated from dilute methanol in rhombs (0.6 g.), m. p. 137°, with a red-brown ferric reaction [Found : C, 66.7; H, 5.2; OMe, 21.3. C₁₄H₁₀O₃(OMe)₂ requires C, 66.7; H, 5.6; OMe, 21.5%]. By the methyl sulphate-potassium carbonate method this was converted into 3: 5-dimethoxybenzyl 2: 4-dimethoxyphenyl ketone, m. p. 107° after purification from methanol (Found : C, 68.4; H, 6.4. C₁₈H₂₀O₅ requires C, 68.4; H, 6.4%).

Reduction of this ketone by Clemmensen's method furnished the diphenylmethane in needles, m. p. 50°, undepressed on admixture with a "natural" specimen, m. p. 51–52° (Found : C, 71·4; H, 7·5. Calc. for $C_{18}H_{22}O_4$: C, 71·5; H, 7·3%).

In attempts to synthesise the tetramethyl ether of the hydroxystilbene, α -(3: 5-dimethoxyphenyl)-2: 4-dimethoxycinnamonitrile was prepared by the condensation of 2: 4-dimethoxybenzaldehyde (1 g.) and 3: 5-dimethoxybenzyl cyanide³ (1 g.) in alcohol (250 ml.) with sodium ethoxide (5 ml. of 5% alcoholic solution) at room temperature for 1 hr. In almost quantitative yield this *nitrile* crystallised from alcohol in yellow needles, m. p. 120° (Found : C, 69.6; H, 5.8; N, 4.4. C₁₉H₁₉O₄N requires C, 70.1; H, 5.8; N, 4.3%). Attempts to hydrolyse this compound with acidic or alkaline reagent gave intractable products.

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Adams, McKenzie, and Lowe, ibid., 1948, 70, 664.