

solution was filtered from potassium chloride and the filtrate concentrated to a syrup, which was fractionated *in vacuo*. The cyanohydrin boiled at 110° at 15 mm. The yield was 20 g.

β -Chloropropionic Acid.—10 g. ethylene cyanohydrin were heated in a sealed tube with 75 cc. concentrated hydrochloric acid at 100° for three hours. Ammonium chloride separated from the solution on cooling. The contents of the tube were diluted with water and extracted with ether. The ethereal extract was dried over sodium sulfate and concentrated, yielding a syrup which easily crystallized. The yield of β -chloropropionic acid so obtained was 10.5 g. Recrystallized from hot ligroin, the acid melted at 38.5–39.5° (corr.) with slight preliminary softening. It possessed the characteristic odor and other properties of β -chloropropionic acid.

0.1964 g. subst.; 0.2560 g. AgCl.

Calc. for $C_3H_5O_2Cl$: Cl, 32.68%. Found: Cl, 32.25%.

β -Bromopropionic Acid.—10 g. ethylene cyanohydrin were boiled with 100 cc. hydrobromic acid (d. 1.49) for three hours. The mixture was cooled, diluted with water, and extracted with ether. The dried ethereal extract yielded on concentration 17 g. β -bromopropionic acid. As so obtained the substance is practically pure. Recrystallized from hot ligroin it melted at 60–61° (corr.) and possessed the recorded properties of β -bromopropionic acid.

0.1554 g. subst.; 0.1910 g. AgBr.

Calc. for $C_3H_5O_2Br$: Br, 52.24%. Found: Br, 52.30%.

NEW YORK CITY.

[CONTRIBUTION FROM THE BUREAU OF CHEMISTRY, U. S. DEPARTMENT OF AGRICULTURE.]

GINGEROL AND PARADOL.¹

By E. K. NELSON.

Received May 1, 1917.

The pungent principles of ginger and of grains of paradise (*amomum melegueta*) were first separated and studied by Thresh.²

Thresh describes both principles as pungent oils which possess the properties of phenols.

To the pungent principle of ginger he assigned the name "Gingerol" and to the similar principle in grains of paradise the name "Paradol." Neither substance was obtained in a state of purity, nor were any crystalline derivatives prepared from them.

¹ While engaged in this research it came to the attention of the writer that Dr. Lapworth, of Manchester, has made a study of gingerol, has isolated its pungent constituent, established its constitution and synthesized it. (*Pharm. J.*, [4] 44, 201.) Accordingly the work here recorded was discontinued and the results published in their present form.

² *Pharm. J.*, [3] 10, 171 (1879); [3] 12, 721 (1881); [3] 14, 798 (1883); [3] 15, 208, (1884).

An investigation of gingerol was undertaken by Garnett and Grier.¹ They distilled the crude gingerol, obtained by extraction methods, under reduced pressure and obtained a pungent oil boiling at 235–240° at 18 mm. As there was evidence of some decomposition during the distillation, they did not feel assured that the distilled product was unchanged gingerol. However its chemical behavior led them to think that it was probably the unchanged substance.

Brooks,² as a result of his work on the volatile oil of ginger, concluded that gingerol has no existence in fact. As Brooks attempted to get gingerol from the volatile oil, and as the pungent principle of ginger is not volatile with steam, it is not surprising that he failed to find it.

It is evident that he overlooked the essential details of the work of Garnett and Grier, and that he was not aware of the work of Thresh on the subject.

Thresh found that gingerol and paradol are very similar. Both are viscid, straw-colored oils, very pungent, reacting like phenols, and readily soluble in 50% alcohol, ether, chloroform and benzene. They are soluble in dilute solutions of sodium or potassium hydroxide, and are precipitated from their alkaline solutions by carbon dioxide. Both substances are moderately soluble in hot petroleum ether, from which they separate on cooling.

Experimental.

Extraction of Gingerol.—Gingerol was isolated by the methods of Thresh and Garnett and Grier. Six kg. of powdered No. 1 African ginger were exhausted with 95% alcohol and the percolate concentrated to a volume of one litre. An equal volume of water was added which caused the precipitation of a large part of the fats and resins, leaving most of the gingerol in solution. The solution was shaken out with petroleum ether and evaporated and the residue extracted by repeatedly boiling out with petroleum ether from which the gingerol was removed by shaking with 60% alcohol.

On evaporating the alcohol gingerol was obtained as a very pungent, yellow oil.

$$d_{20}^{20} = 1.0713, [\alpha]_D^{20} = +12.9^{\circ}, n_D^{20} = 1.5212.$$

By the Zeisel method gingerol was found to contain 9.26% CH₃O.

Extraction of Paradol.—2.2 kg. of powdered grains of paradise were exhausted with 95% alcohol and the concentrated alcoholic extract distilled with steam to remove volatile oils. The residue was dissolved in 50% alcohol. The resins were precipitated with an excess of basic lead acetate, and filtered off. After removing the excess of lead from the filtrate it was evaporated and the residue boiled out repeatedly with

¹ *Pharm. J.*, [4] 25, 118 (1907).

² *THIS JOURNAL*, 38, 430 (1916); *Dissertation*, Göttingen, 1912.

petroleum ether. From the petroleum ether solutions the paradol was removed by shaking out with 60% alcohol, and on evaporating the alcohol paradol was obtained as a yellow pungent oil.

$$d_{20}^{20} = 1.0690, [\alpha]_D = +9.2^\circ, n_D^{20} = 1.5232, \text{CH}_3\text{O} = 10.93\%.$$

Gingerol was found to be the substance in ginger which gives the Seeker¹ test.

If a small quantity of gingerol is mixed with vanillin and sulfuric acid and the mixture diluted with a small amount of water an intense azure blue color develops. On applying this test to paradol it was found to give the same reaction.

The benzoates of gingerol and paradol were prepared but could not be obtained in crystalline form.

Methylation of Gingerol and Paradol.—No difficulty was experienced in obtaining a crystalline methyl derivative from these pungent substances. 18.7 g. of gingerol were mixed with 15 g. of dimethyl sulfate in a 500 cc. flask and 300 cc. of a 5% solution of sodium hydroxide were carefully added, while shaking, and the mixture well agitated for an hour. On adding a little dilute sulfuric acid the product separated in crystalline form, and was filtered on a Büchner funnel, dried and recrystallized from hot petroleum ether.

A yield of 43% of the crystalline compound was obtained. A liquid product was also formed, the yield being 50% of the weight of gingerol taken.

The methyl ether of gingerol crystallizes from petroleum ether in groups of white needles or prisms melting at 65–65.5°.

Paradol, on methylating, also afforded a crystalline product and an oil. The methyl ether of paradol also melts at 65–65.5°, is identical in crystalline form with methyl gingerol, and a mixture of the two products shows no depression in melting point. Hence they are identical.

0.6325 g. in 10 cc. alcohol at 20° in 100 mm. tube = +0.59°; $[\alpha]_D = +9.3^\circ$.

Calc. for $\text{C}_{17}\text{H}_{24}\text{O}_2(\text{OCH}_3)_2$: C, 70.8%; H, 9.4%; CH_3O , 19.3%; mol. wt., 322. Found: C, 70.6, 70.9, 70.6%; H, 9.5, 9.7, 9.8%; CH_3O , 20.0%; mol. wt., 321, 323.

The liquid products formed on methylating are not pungent and are probably mixtures of the crystalline methyl ester with a liquid derivative which may be a homologue.

The dimethyl ether is not pungent, but on splitting off the added methyl group by boiling with aluminium chloride in benzene solution a very pungent oil is obtained, thus showing the methyl compound to be a derivative of the pungent substance.

The oil thus regenerated is quite unstable and polymerizes readily to a red resin insoluble in petroleum ether.

¹ Bureau Chem., *Circ.* 66, p. 22.

Distillation of Gingerol and Paradol.—Gingerol was distilled and the distillate fractionated at 6 mm. In the first distillation there was evidence of partial decomposition and a resinous residue was left in the flask. In two subsequent fractionations of the distillate this decomposition was not so marked, and the main fraction was obtained as an oil boiling at 227–229° at 6 mm. This oil is not quite so pungent as the original gingerol. It gives a strong Seeker test, reacts as a phenol, and in alcoholic solution gives a green color with ferric chloride.

$$d_{20} = 1.0503, [\alpha]_D = \pm 0, n_D^{25} = 1.5242.$$

Calc. for $C_{16}H_{21}O_2(OCH_3)$: C, 72.6%; H, 9.1%; CH_3O , 11.7%; mol. wt., 264. Found: C, 72.5, 72.9, 72.8%; H, 9.0, 9.2, 8.9%; CH_3O , 10.7%; mol. wt., 270, 277.

The distilled product on methylating does not yield a crystalline methyl ether, and is optically inactive, thus differing from the original gingerol.

Paradol, on distillation, behaved like gingerol, and an oil was obtained boiling at 230–234° at 8 mm.

$$d_{20}^{20} = 1.0415, [\alpha]_D = \pm 0, n_D^{20} = 1.5198.$$

Calc. for $C_{16}H_{21}O_2(OCH_3)$: C, 72.6%; H, 9.1%; CH_3O , 11.7%; mol. wt., 264. Found: C, 73.0, 73.0%; H, 9.0, 9.2%; CH_3O , 11.2, 11.1%; mol. wt., 266, 277.

The properties of distilled paradol are identical with those of distilled gingerol. No crystalline methyl derivative could be obtained from it.

Discussion.

Up to this point the evidence of the identity of gingerol and paradol is very strong. However, they differ in their stability on boiling with alcoholic potassium hydroxide. Equal weights of gingerol and of paradol were boiled for an hour with 50 cc. 2 *N* alcoholic potassium hydroxide. Under these conditions the pungency of the gingerol is destroyed or very much diminished, whereas the pungency of paradol is little affected.

As the results indicate that gingerol and paradol are monomethyl ethers of dihydric phenols, this difference in properties may be accounted for by a difference in the positions of the methyl group.

Both pungent principles as extracted from the spices are evidently not homogeneous but consist of mixtures of the substance yielding a crystalline dimethyl ether with one or more substances yielding liquid methyl ethers.

The composition of the substance yielding the crystalline dimethyl ether would be represented by the formula

