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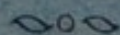
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ACTION OF SODIUM AMALGAM
ON
METHYLENE ETHERS

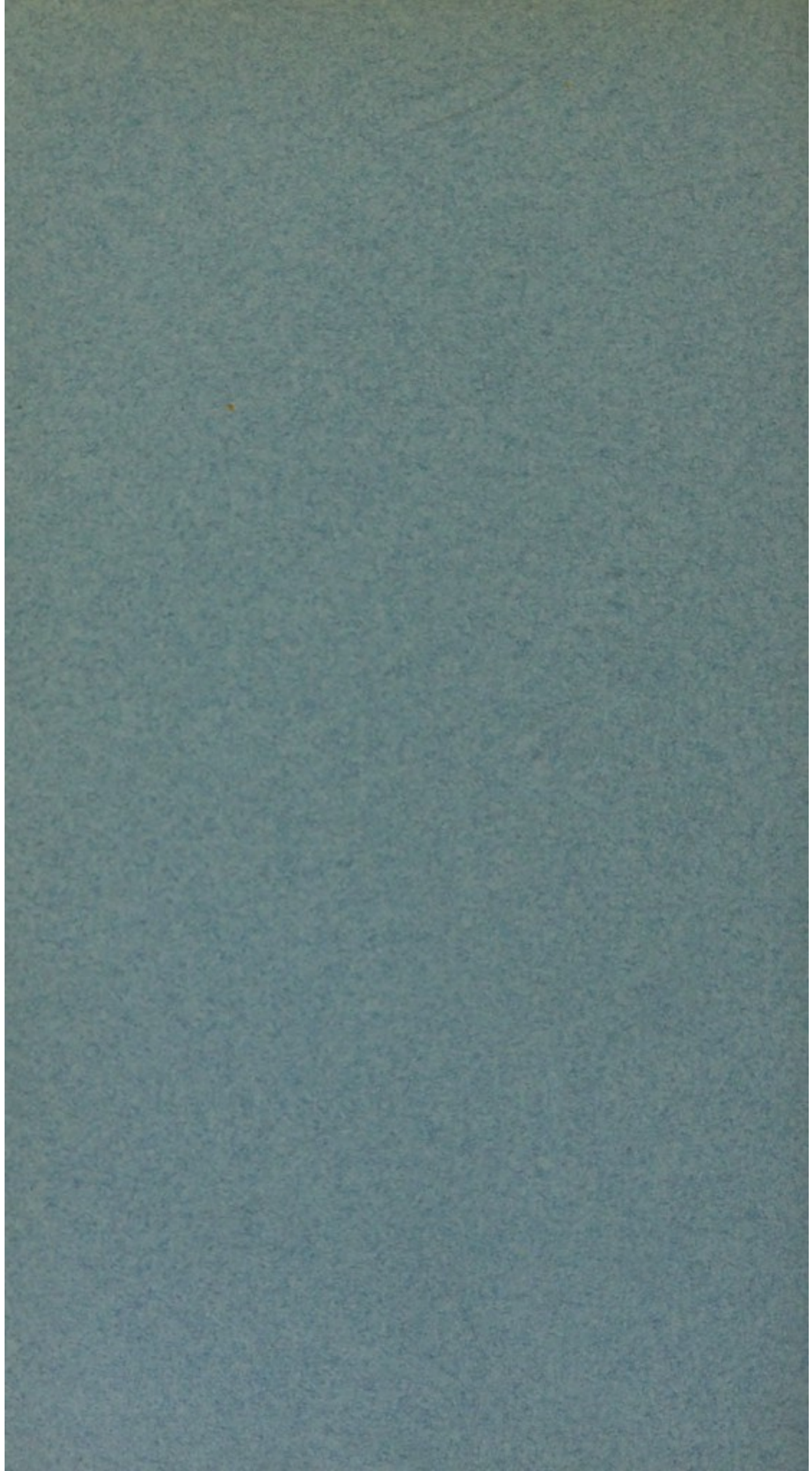
BY

ARTHUR H. SALWAY, PH.D., D.SC.

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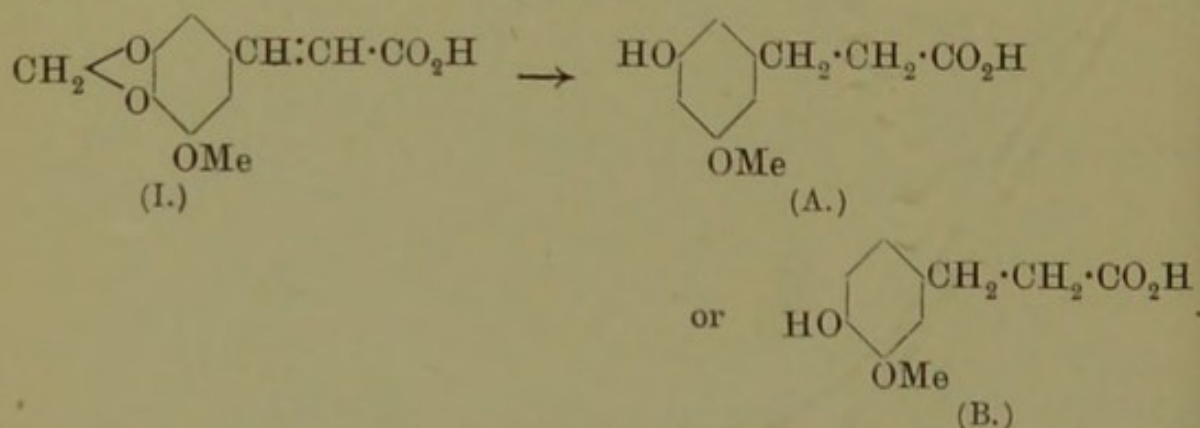
CCXLVII.—*Action of Sodium Amalgam on Methylene Ethers.*

By ARTHUR HENRY SALWAY.

IN the course of the author's previous investigations, which led to the synthesis of cotarnine (Trans., 1909, **95**, 1204; this vol., 1208), the reduction of 3-methoxy-4:5-methylenedioxcinnamic acid (I) was described. In this reaction it was observed that the normal reduction product, namely, β -3-methoxy-4:5-methylene-dioxyphenylpropionic acid (II), was invariably accompanied by a considerable proportion of a by-product. This substance, of which

no account was given in the previous communications, has now been isolated in sufficient quantity to render its complete examination possible.

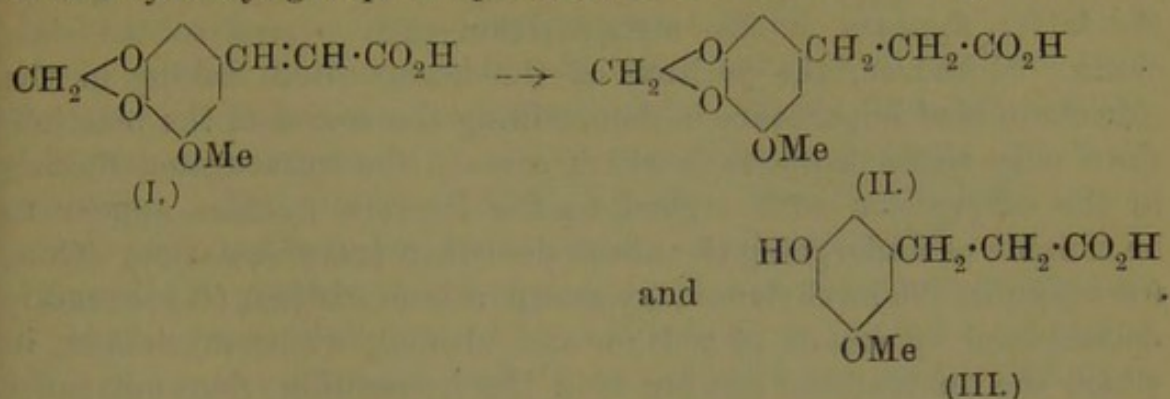
The purified compound was found to possess the properties of a phenol and of a carboxylic acid, and gave analyses corresponding with the empirical formula $C_{10}H_{12}O_4$. It is evident that the production of such a compound from 3-methoxy-4:5-methylenedioxy-cinnamic acid (I) can only be explained by the simultaneous reduction of the aliphatic side-chain and the substitution of a hydroxyl group for the methylenedioxy-complex. The constitution of the resulting compound would therefore appear to be represented by one of the two formulæ A and B:



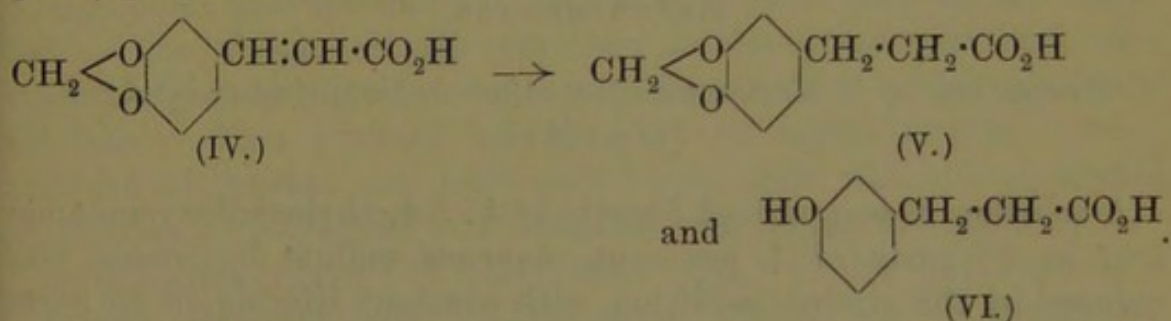
In order to decide between these formulæ, the substance was converted by means of methyl sulphate into a dimethoxyphenylpropionic acid, which melted at 61—62°. The dimethoxy-acid corresponding with B, namely, β -3:4-dimethoxyphenylpropionic acid, melts, according to Tiemann and Nagai (*Ber.*, 1878, 11, 653), at 97°, whilst the 3:5-dimethoxy-acid corresponding with A does not appear to have been hitherto described. Formula B is thus shown to be inadmissible, and consequently A most probably represents the constitution of the substance under examination. Positive evidence in support of this conclusion was obtained by converting the dimethoxypropionic acid into the corresponding dimethoxybenzoic acid by oxidation with alkaline permanganate solution. The product of oxidation melted at 180—181°, and was found to be identical with 3:5-dimethoxybenzoic acid. It is thus shown that in the reduction of 3-methoxy-4:5-methylenedioxy-cinnamic acid (I), the normal reaction is accompanied by a secondary change involving the disruption of the methylenedioxy-complex and the formation of β -5-hydroxy-3-methoxyphenylpropionic acid (III), according to the scheme on p. 2415.

It was next deemed of interest to ascertain whether other methylene ethers are capable of undergoing a similar change, and accordingly piperonylacrylic acid (IV) was subjected to the action of sodium amalgam. In this case, also, it was found that reduction

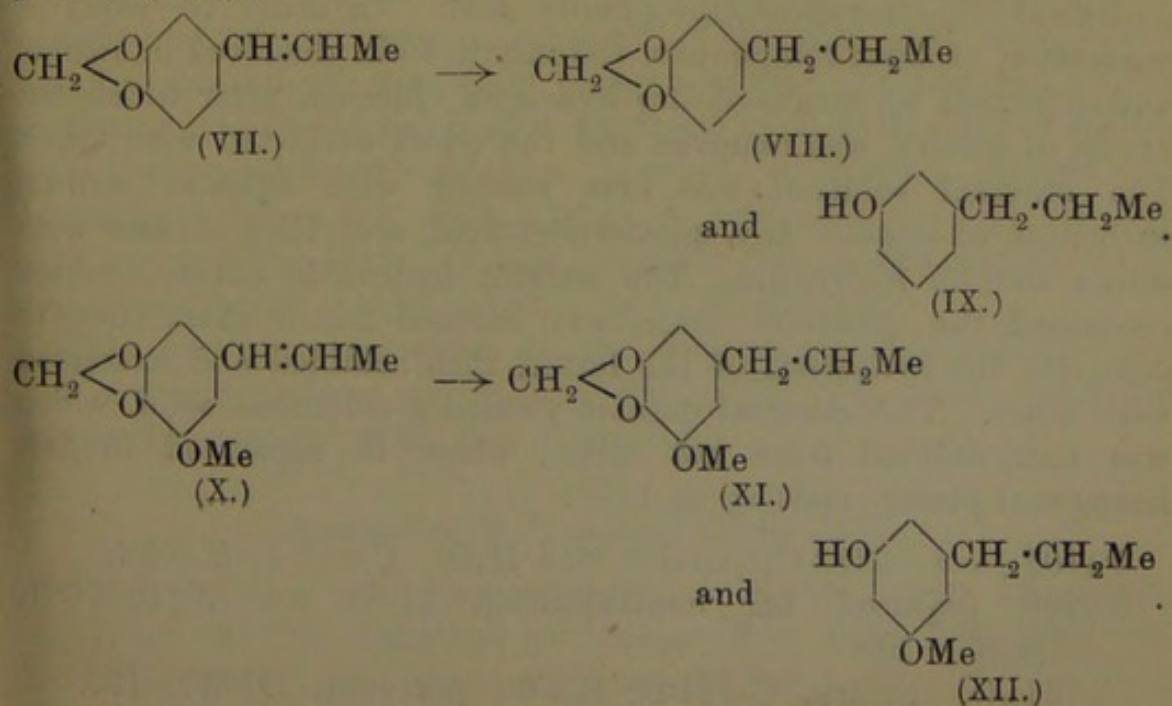
takes place with partial conversion of the methylenedioxy-complex into a hydroxyl group, the products of the reaction being a mixture



of β -3: 4-methylenedioxyphenylpropionic acid (V) and β -3-hydroxyphenylpropionic acid (VI):



A similar reaction has been observed by Ciamician and Silber (*Ber.*, 1890, **23**, 1162), who have shown that *isosafrole* (VII), when reduced by sodium and alcohol, is converted into a mixture of 3: 4-methylenedioxypropylbenzene (VIII) and *m*-propylphenol (IX), whilst Thoms (*Ber.*, 1903, **36**, 3449) records the fact that *isomyristicin* (X), under similar conditions, yields both 5-methoxy-3: 4-methylenedioxypropylbenzene (XI) and 5-methoxy-3-propylphenol (XII):



It is worthy of note that in each of the above examples of the displacement of a methylenedioxy-complex by a hydroxyl group, the latter appears in the meta-position with regard to the side-chain. Moreover, the position of the unsaturated linking in the side-chain is of importance in determining the course of the reaction, since only those compounds which contain the unsaturated linking in the $\alpha\beta$ -position with regard to the benzene nucleus appear to be capable of undergoing the above-described transformation. Thus, for example, the methylenedioxy-group of *isomyristicin* (X) is readily decomposed by means of sodium and alcohol, whilst *myristicin*, in which the unsaturated linking is in the $\beta\gamma$ -position, does not suffer this change.

EXPERIMENTAL.

Reduction of 3-Methoxy-4:5-methylenedioxybenzoic Acid (I, p. 2415).

A solution of one part of 3-methoxy-4:5-methylenedioxybenzoic acid in 20 parts of 1 per cent. aqueous sodium hydroxide was reduced by the gradual addition, with constant stirring, of 16 parts of sodium amalgam (4 per cent.). After the amalgam had been completely decomposed, the mixture was acidified, the precipitated oil extracted with ether, and the ethereal solution washed, dried, and the solvent removed. In this manner the product of reduction was obtained as a light brown oil, which gradually became crystalline. A preliminary examination of the product indicated the presence of a considerable proportion of a phenolic carboxylic acid in addition to the normal reduction product, β -3-methoxy-4:5-methylenedioxyphenylpropionic acid. In order to effect a separation of these compounds, the mixture was dissolved in alcohol and esterified by means of dry hydrogen chloride, after which the excess of alcohol was removed and the esters extracted with ether. The ethereal solution was first washed with aqueous sodium carbonate to remove any unesterified acid, and then shaken with dilute sodium hydroxide. The sodium hydroxide extract, which contained the phenolic ester, was warmed for a short time to complete the hydrolysis of the latter, then acidified and extracted with ether. This ethereal extract yielded a colourless solid, which was recrystallised from hot water, when it separated in flat, hexagonal plates, melting at 127° :

0.1103 gave 0.2482 CO_2 and 0.0635 H_2O . $\text{C} = 61.4$; $\text{H} = 6.4$.

0.2800 required for neutralisation 14.35 c.c. $N/10\text{-KOH}$.

M.W. = 195.

$\text{C}_{10}\text{H}_{12}\text{O}_4$ requires $\text{C} = 61.2$; $\text{H} = 6.1$ per cent. M.W. = 196.

As already explained in the introduction, this substance was found to be β -5-hydroxy-3-methoxyphenylpropionic acid.

β -5-Hydroxy-3-methoxyphenylpropionic acid (III, p. 2415) is readily soluble in ether, alcohol, or hot water, and crystallises from the latter in colourless, hexagonal plates, which gradually become pink on exposure to air. It is insoluble in benzene or light petroleum. Its *amide*, $\text{MeO} \cdot \text{C}_6\text{H}_3(\text{OH}) \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CO} \cdot \text{NH}_2$, crystallises from water in prismatic needles, melting at 126° .

In order to prepare the methyl derivative of the above compound, 10 grams of the phenolic acid were dissolved in methyl alcohol and 5 c.c. of methyl sulphate, and 10 c.c. of a 50 per cent. solution of potassium hydroxide added. After the vigorous reaction had subsided, the same quantities of methyl sulphate and alkali were again added, and the mixture heated for a short time on the water-bath. The alkaline liquid was then acidified and extracted with ether, when the ethereal extract yielded an oil which gradually solidified. This product was purified by crystallisation from a mixture of benzene and light petroleum, from which it separated in clusters of colourless, silky needles, melting at $61\text{--}62^\circ$:

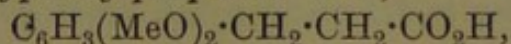
0.1076 gave 0.2490 CO_2 and 0.0649 H_2O . $\text{C} = 63.1$; $\text{H} = 6.7$.

0.4465 required for neutralisation 21.25 c.c. $N/10\text{-NaOH}$.

M.W. = 210.

$\text{C}_{11}\text{H}_{14}\text{O}_4$ requires $\text{C} = 62.9$; $\text{H} = 6.7$ per cent. M.W. = 210.

β -3: 5-Dimethoxyphenylpropionic acid,



is readily soluble in the usual organic solvents, excepting light petroleum. It yields an *amide*, which crystallises from a mixture of benzene and petroleum in colourless needles, melting at $80\text{--}81^\circ$. The position of the methoxy-groups in the above compound was ascertained by oxidising a quantity of the substance with a hot alkaline solution of potassium permanganate. At the end of the oxidation, the liquid was cooled, an excess of sulphur dioxide added, and the precipitated oxidation product collected. It was recrystallised from hot water, when it separated in thin needles, melting at $180\text{--}181^\circ$. (0.2045 required for neutralisation 11.25 c.c. $N/10\text{-NaOH}$. M.W. = 182. Calc., M.W. = 182.)

This substance possessed all the properties of 3: 5-dimethoxybenzoic acid (Bülow and Riess, *Ber.*, 1902, **35**, 3901), and was evidently identical with that compound.

Reduction of Piperonylacrylic Acid.

The reduction of piperonylacrylic acid by means of sodium amalgam was first described by Lorenz (*Ber.*, 1880, **13**, 758), who isolated piperonylpropionic acid from the product of the reaction,

but did not record the formation of a phenolic compound. In view, however, of the results obtained in the above reduction of 3-methoxy-4:5-methylenedioxybenzoic acid, it seemed probable that some β -5-hydroxyphenylpropionic acid would be formed in the reduction of piperonylacrylic acid. In order to ascertain if this were the case, 20 grams of piperonylacrylic acid were reduced with sodium amalgam in the manner described in connexion with the reduction of 3-methoxy-4:5-methylenedioxybenzoic acid. The product was then esterified, and, by means of dilute sodium hydroxide, separated into a non-phenolic and a phenolic ester. The former amounted to 18 to 19 grams, and yielded on hydrolysis piperonylpropionic acid, melting at 85° , whilst the latter, when hydrolysed, yielded a brown oil (2 grams), which gradually solidified on agitation with benzene. This substance was purified by recrystallisation from a mixture of ether and benzene, and was thus obtained in colourless needles, melting at 110° . (0.1922 required 11.8 c.c. $N/10$ -NaOH for neutralisation. M.W.=163. Calc., M.W.=166.)

This compound possessed all the properties of 3-hydroxyphenylpropionic acid, and was evidently identical with it (Braunstein, *Ber.*, 1882, 15, 2050).

The action of sodium amalgam on piperonylacrylic acid is therefore analogous to that which takes place when 3-methoxy-4:5-methylenedioxybenzoic acid is reduced. The yield of phenolic acid in the latter case is, however, much greater than in the former.

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