acid containing reducing agents such as sulfur dioxide. It decomposes hydrogen peroxide without itself being changed. It oxidizes alcohols to the corresponding aldehydes.

4. It has been shown that the nitrates of lithium, potassium, calcium, barium and strontium are not nearly so satisfactory for the fusion with chloroplatinic acid as sodium nitrate.

5. A comparison of the catalytic activity of this oxide with the various oxides obtained by methods described in the literature has shown the former to be far superior. Moreover, it is much more readily prepared.

Urbana, Illinois

[Contribution from the Chemical Warfare Service[1] and the Bureau of Chemistry, United States Department of Agriculture]

THE CONSTITUTION OF CAPSAICIN, THE PUNGENT PRINCIPLE OF CAPSICUM. III

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Received July 2, 1923

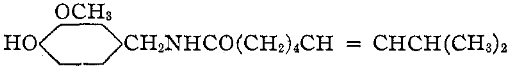
In former contributions by one of us[2] capsaicin was shown to be the vanillyl amide of a decenic (decylenic) acid. Beyond proof that this decenic acid is not a straight-chain acid, its constitution remained undetermined. The primary purpose of the present work was to determine the structure of this acid, thereby establishing the complete structure of capsaicin.

On account of the scarcity of material at the time, it was decided to attack the problem from the synthetic end, which required, of course, the synthesis of a considerable number of 10-carbon acids. In order to simplify the work, the question of the location of the double bond was deferred for the time being, and a saturated acid was sought which, when condensed with vanillyl amine, would give a product identical with that obtained on hydrogenating the side chain of capsaicin.

Such an acid was finally found in 8-methyl-nonoic acid, which has been described by Levene and Allen.[3]

The location of the double bond in the decenic acid from capsaicin was finally determined by its oxidation with a 5% solution of potassium permanganate, the products being adipic acid and *iso*butyric acid.

This shows that the double bond is located between the sixth and seventh carbon atoms, and that capsaicin is the vanillyl amide of Δ^6, 8-methylnonenic acid,



$$\mathrm{HO}\overset{\mathrm{OCH_3}}{\langle\qquad\rangle}\mathrm{CH_2NHCO(CH_2)_4CH = CHCH(CH_3)_2}$$

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[1] Released by Chemical Warfare Service.

[2] Nelson, This Journal, 41, 1115 (1919); 42, 598 (1920).

[3] Levene and Allen, *J. Biol. Chem.*, 27, 433 (1916).

Experimental Part

Hydrogenated Capsaicin.—One g. of capsaicin, dissolved in absolute alcohol, when shaken in the presence of hydrogen with 0.05 g. of colloidal palladium, absorbed 2 atomic proportions of hydrogen within 10 hours. The product, recrystallized from petroleum ether, melted at 65°. Its solution in chloroform did not decolorize a dilute solution of bromine in the same solvent, whereas a solution of capsaicin immediately decolorizes bromine. The appearance and optical properties[4] of hydrogenated capsaicin are very similar to those of capsaicin. The refractive indices, $n_D^{20°}$ of the two compounds determined by the immersion method in potassium mercuric iodide solution were as follows.

	α	β	γ
Capsaicin	1.520	1.540	1.580
Hydrogenated capsaicin	1.510	1.520	1.555

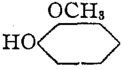
In a second experiment, 0.6855 g. of the saturated acid, made by hydrogenating the decenic acid from capsaicin, was converted into the chloride and then condensed with vanillyl amine. The resulting product had the same physical and optical properties as the hydrogenated capsaicin and did not show unsaturation with very dilute solution of bromine.

Synthesis of 8-Methyl-nonoic Acid.—Ethyl *iso*caproate (110 g.) was reduced to 4-methyl-pentyl alcohol by the method of Levene and Allen.[3] The yield of 4-methyl-pentyl alcohol, boiling at 150–152°, amounted to 52.3 g., or 67.3% of the calculated amount. This 4-methyl-pentyl alcohol (52.3 g.) was refluxed for 3 hours with 4 molecular proportions of hydriodic acid (b. p., 127°) and the resulting iodide was separated and rectified. A yield of 97.8 g. (90%) of 4-methyl-pentyl iodide was obtained. The 4-methyl-pentyl iodide was then condensed with aceto-acetic ester according to the method of Locquin,[5] yielding 83 g. of 4-methyl-pentyl aceto-acetic ester, boiling at 155–160° (20 mm.).

The 4-methyl-pentyl aceto-acetic ester (83 g.) was saponified by the method of Dieckmann,[6] which consisted in boiling it for 4 hours with 10 g. of sodium dissolved in 250 cc. of absolute alcohol. The resulting ethyl 6-methyl-heptylate, boiling at 201–203°, was obtained in a yield of 66.2%. At this point some unchanged material from previous operations was recovered and converted into ethyl 6-methyl-heptylate.

Ethyl 6-methyl-heptylate was reduced by the Levene-Allen method and 33.9 g. of 6-methyl-heptyl alcohol, boiling at 185–190°, was obtained. The corresponding iodide was prepared, with a yield of 56.3 g., boiling at 100–105° (17 mm.). This was condensed with aceto-acetic ester, affording ethyl 8-methyl-nonoate which, on being saponified, gave a yield of 27.4 g. of 8-methyl-nonoic acid, boiling at 150° (15–16 mm.).

Preparation of 8-Methyl-nonoyl Vanillyl Amide,



$\overset{OCH_3}{HO\langle\quad\rangle}CH_2.NH.CO(CH_2)_6.CH(CH_3)_2$.—The 8-methyl-nonoic acid (1.18 g.) was converted into the acid chloride, and the latter condensed with vanillyl amine. The 8-methyl-nonoyl vanillyl amide formed melted at 65° and a mixture with hydrogenated capsaicin gave no depression in melting point. Its optical properties were also identical with those of hydrogenated capsaicin.

The pungency of the synthetic product, as well as that of hydrogenated capsaicin, was proved by direct quantitative experiment to be as great

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[4] The optical measurements were kindly made by Dr. Edgar T. Wherry of the Bureau of Chemistry.

[5] Locquin, *Bull. soc. chim.*, [3] 31, 757 (1904).

[6] Dieckmann, *Ber.*, 33, 2670 (1900).

as the pungency of capsaicin. This shows that the double bond exerts little or no influence on pungency, which is contrary to the assumption of Ott and Zimmermann[7] that unsaturation in the side chain of capsaicin and related compounds is necessary for pungency. The preparation of the vanillyl amides of other synthetic saturated and unsaturated acids, the description of which is reserved for a later communication, has also disproved the assumption that unsaturation in the side chain is a requirement of pungency.

Oxidation of the Decenic Acid from Capsaicin.—The acid isolated from the capsaicin by heating it to 180° with a 25% solution of sodium hydroxide was oxidized in the cold with a 5% solution of potassium permanganate. A partially crystalline product was thus obtained. This was separated by distillation with steam into a non-volatile, crystalline acid and a volatile, liquid acid.

The crystalline acid melted at 147–150° (adipic acid melts at 149–149.5°). 0.1703 g. of the silver salt yielded 0.1017 g. of silver, or 59.7%; calculated for silver adipate, 59.96%.

The volatile, liquid acid was also converted into the silver salt which was found to contain 54.99% of silver; calculated for silver *iso*butyrate, 55.34%. This was known to be *iso*butyric acid on account of our knowledge of the structure of the corresponding saturated acid. The decenic acid from capsaicin is thus shown to have the double bond between the sixth and seventh carbon atoms and is therefore Δ^6, 8-methyl-nonenic acid.

Summary

Hydrogenated capsaicin has been prepared and found to be very similar to capsaicin in all its properties, except that it does not decolorize a dil. bromine solution and differs in the refractive indices of its crystals.

A compound identical in all respects with hydrogenated capsaicin was prepared by condensing 8-methyl-nonoic acid with vanillyl amine.

A study of this compound has shown that it is quite as pungent as capsaicin and that the double bond is not necessary for pungency.

The unsaturated acid from capsaicin has been found to have its double bond in the 6 position, thus showing that capsaicin is Δ^6, 8-methyl-nonenyl vanillyl amide.

WASHINGTON, D. C.

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[7] Ott and Zimmermann, *Ann.*, **425**, 314 (1921).