[CONTRIBUTION FROM THE ESSENTIAL OILS LABORATORY, DRUG DIVISION, BUREAU OF CHEMISTRY, U. S. DEPARTMENT OF AGRICULTURE.]

VANILLYL-ACYL AMIDES.

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The investigation in this laboratory of the constitution of capsaicin,¹ which demonstrated that substance to be a vanillyl-decenoyl amide, has led to the synthesis of a number of other vanillyl-acyl amides (4-hydroxy-3-methoxy-benzyl-acyl amides), of the type (4)HO(3)CH₃OC₆H₃(1)CH₂-NHCOR.

Vanillyl amine, suspended in dry ether, reacts readily with acyl chlorides, forming vanillyl-acyl amides, which are substances of the capsaicin type.

General Method of Preparation.

A quantity of vanillyl amine corresponding to two molecules, freed from its water of crystallization by heating at 110°, is suspended in dry ether, and a quantity of the acyl chloride corresponding to one molecule is added, the mixture being stirred meanwhile. The mixture is then heated gently to complete the reaction, water and a little hydrochloric acid are added, and the mixture is shaken out in a separatory funnel, the aqueous layer being drawn off. In case acids of low molecular weight, up to hexoic acid, are being used, it is necessary to extract the aqueous solution thoroughly with chloroform and add this to the ether solution, as the derivatives of the lower acids are soluble in water and insoluble, or difficultly soluble, in ether. The aqueous solution is then evaporated to recover the excess of vanillyl amine in the form of the hydrochloride. The ether or chloroform-ether solution is washed with a dilute solution of sodium carbonate, to remove any uncombined acid, and evaporated.

The condensation product thus obtained is purified by crystallizing from a suitable solvent, usually benzene for the lower members of the series, or petroleum ether containing some ethyl ether for the higher ones.

The acyl chlorides are prepared as needed by adding to the weighed amount of acid the required quantity of phosphorus trichloride, heating gently and decanting the acyl chloride directly from the viscous deposit of phosphorous acid.

The foregoing method of preparation was employed for all the substances to be described, with the exception of the acetyl and isobutyryl derivatives, which were made by the use of the corresponding acid anhydrides.

Derivatives of the Acids of the Acetic Acid Series.

Vanillyl Acetamide.—10 g. of vanillyl amine, 20 g. of acetic anhydride and one g. anhydrous sodium acetate were heated for 4 hours at 130° . An excess of sodium hydroxide was added to the cooled mixture and after shaking and saturation with carbon dioxide the solution was thoroughly

¹ Nelson, This Journal, 41, 1115 (1919).

extracted with chloroform. The residue from evaporation of the chloroform was saponified with cold alcoholic potassium hydroxide, in order to remove the acetyl group substituted in the hydroxyl of the vanillyl residue, diluted with water, saturated with carbon dioxide and extracted with chloroform. On evaporating the chloroform the compound remained as a thick brown syrup which slowly became crystalline. Recrystallized from boiling benzene it melted at $84-5^{\circ}$ (corr.). The yield was 62%.

Calc. for $C_{10}H_{13}NO_3$: C, 61.5; H, 6.7; N, 7.17.

Found: C, 61.6; H, 6.9; N, 7.12.

Vanillyl acetamide is easily soluble in water and in chloroform but is insoluble in ether. It is not pungent.

Optical-crystallographic Data¹—In ordinary light, vanillyl acetamide is seen to consist of rods breaking into irregular fragments, the crystal system being monoclinic. The refractive indices (determined by the immersion method, using mixtures of lubricating oil with monobromonaphthalene and of the latter with methylene iodide) are: $\alpha = 1.550$, $\beta = 1.585$, $\gamma = 1.685$, $\gamma - \alpha = 0.135$, all ± 0.005 . Intermediate values are usually obtained. In parallel polarized light, nicols crossed: The birefringence is extreme, the colors being of high orders. Extinction is inclined, reaching a maximum of 30°; elongation is variable. In convergent polarized light, nicols crossed: Partial biaxial figures are often obtained, the axial plane running lengthwise, the apparent axial angle 2E being about 110° (calc. 115°) and the sign positive. The dispersion is distinct.

Vanillyl Propionamide.—2.5 g. of propionic acid was converted into the chloride and added to 10.3 g. of vanillyl amine suspended in ether. The derivative was recrystallized from hot benzene and melted at 108– 10° (corr.). The yield was 46%.

> Calc. for C₁₁H₁₅NO₈: C, 63.1; H, 7.2; N, 6.69. Found: C, 63.3; H, 7.2; N, 6.67.

Vanillyl propionamide is scarcely soluble in ether but is soluble in water, chloroform or hot benzene. Its aqueous solution is very slightly pungent.

Optical-crystallographic Data.—In ordinary light, vanillyl propionamide is in short rods and irregular grains, the system being rhombic. Refractive indices, determined as in the preceding substance: $\alpha = 1.495$, $\beta = 1.635$, $\gamma = 1.680$, $\gamma - \alpha = 0.185$, all ± 0.005 ; intermediate values are usually obtained. In parallel polarized light, nicols crossed: Birefringence is extreme, the colors being of high orders. Extinction is parallel, and elongation variable. In convergent polarized light, nicols crossed: Partial biaxial figures are occasionally obtained, 2E being about 100° (calc. 98°) and the sign negative. Dispersion is distinct.

Vanillyl *n*-Butyramide.—Normal butyric acid was used and the acid ¹ The optical-crystallographic observations in this paper were kindly made by Dr. Edgar T. Wherry, of the Bureau of Chemistry. chloride method employed. The yield was 44%. Vanillyl *n*-butyramide crystallizes slowly. It was crystallized from benzene and recrystallized from dry ether, when it melted at $68-70^{\circ}$ (corr.).

Calc. for $C_{12}H_{17}NO_8$: C, 64.5; H, 7.7; N, 6.29. Found: C, 64.4; H, 7.6; N, 6.34.

Vanillyl *n*-butyramide is readily soluble in chloroform and moderately soluble in ether and in water. It is somewhat pungent.

Optical-crystallographic Data.—In ordinary light, vanillyl n-butyramide is in minute rods, grains and irregular aggregates, the system being apparently triclinic. Refractive indices: $\alpha = 1.515$, $\beta = 1.580$, $\gamma = 1.655$, $\gamma - \alpha = 0.140$, all ± 0.005 ; intermediate values are usually obtained. In parallel polarized light, nicols crossed: Birefringence is extreme, the colors being of high orders. Extinction is strongly inclined, reaching 45°, and elongation is variable. In convergent polarized light, nicols crossed: Partial biaxial figures are often obtained, 2E being extremely large, and the sign probably positive. Dispersion is distinct.

Vanillyl Isobutyramide.—Isobutyric anhydride was employed. The yield was 80%. Recrystallized from dil. alcohol, vanillyl isobutyramide melted at $118-20^{\circ}$.

Calc. for $C_{12}H_{17}NO_3$: C, 64.5; H, 7.7; N, 6.29.

Found: C, 64.4; H, 7.7; N, 6.15.

Vanillyl isobutyramide is scarcely soluble in ether but is soluble in chloroform and moderately soluble in water. It is only slightly pungent.

Optical-crystallographic Data.—In ordinary light, vanillyl isobutyramide is in rectangular plates and pyramids, the system being rhombic. Refractive indices: $\alpha = 1.465$, $\beta = 1.633$, $\gamma = 1.635$, $\gamma - \alpha = 0.170$, all ± 0.005 . In parallel polarized light, nicols crossed: Birefringence is extreme, the colors being of high orders. Extinction is symmetrical, and elongation variable. In convergent polarized light, nicols crossed: Biaxial figures are often obtained, 2E being very small, about 18° (calc. $17^{\circ} 48'$), and the sign negative. Dispersion is distinct.

Vanillyl *n*-hexoylamide.—Caproic acid made by the fermentation of kelp was used in preparing vanillyl *n*-hexoylamide. The acid was obtained from the Hercules Powder Co., Although it distilled within narrow limits as received, it was converted into the methyl ester and this was carefully fractionated. The fraction boiling at $49-52^{\circ}$ under 15 mm. pressure was saponified, and from this an acid boiling at $103-6^{\circ}$ under 15 mm. pressure was obtained.

Vanillyl *n*-hexoylamide, however, was not obtained in crystalline form and all efforts to induce crystallization failed. It seems probable, therefore, that the caproic acid may not be pure normal acid. The condensation product, as obtained, appears as a light brown, very viscous syrup. It is moderately soluble in boiling water, from which it separates, for the most part, on cooling. It is soluble in ether and in chloroform. Vanilly n-hexoylamide is far more pungent than the lower members of the series.

Vanillyl *n*-Heptoylamide.—Normal heptoic acid was made by the oxidation of oenanthol, which was prepared by distilling castor oil under diminished pressure. The acid boiled at 114° under 10 mm. pressure. By the condensation of *n*-heptoic acid and vanillyl amine, through the acid chloride, a yield of 81% of vanillyl *n*-heptoylamide was obtained. Recrystallized from a mixture of ether and petroleum ether, it melted at 59-61° (corr.).

Calc. for $C_{15}H_{23}NO_3$: C, 67.9; H, 8.7; N, 5.24. Found: C, 67.5; H, 8.7; N, 5.19.

Vanillyl *n*-heptoylamide is very pungent.

Optical-crystallographic Data.—In ordinary light, vanillyl n-heptoylamide is in grains, the system being probably monoclinic. Refractive indices: $\alpha = 1.515$, $\beta = 1.595$, $\gamma = 1.625$, $\gamma - \alpha = 0.110$, all ± 0.005 ; intermediate values are usually obtained. In parallel polarized light, nicols crossed: Birefringence is extreme, the colors being mostly about 3rd order. Extinction is usually strongly inclined, though occasionally symmetrical, and elongation is variable. In convergent polarized light, nicols crossed: Partial biaxial figures are occasionally obtained, 2E being about 110° (calc. 107°), and the sign negative. Dispersion is distinct.

Vanillyl *n*-octoylamide.—Caprylic acid (normal octoic acid) was isolated from coconut oil by carefully fractionating the methyl esters of coconut oil fatty acids. The fraction boiling at 83–6° under 15 mm. pressure was saponified and the acid recovered and rectified.

As a perfectly homogeneous condensation product was not obtained with vanillyl amine, the acid was further purified by fractionally crystallizing its barium salt. The acid thus purified had a constant boiling point and was used in preparing vanillyl *n*-octoylamide, of which a yield of 83% was obtained. Recrystallized from petroleum ether containing 10% of ethyl ether, this compound melted at $41-3^{\circ}$ (corr.).

Cale. for $C_{16}H_{25}NO_3$: C, 68.8; H, 9.0; N, 5.01. Found: C, 68.8; H, 9.1; N, 5.05.

Vanillyl *n*-octoylamide is a violently pungent substance. Care must be taken in handling it that its solutions do not come in contact with the face or with the eyes. Its pungency on the tongue is about equal to that of capsaicin, but its property of causing sneezing and coughing is probably not quite so great.

Optical-crystallographic Data.—In ordinary light, vanillyl n-octoylamide is in very minute needles, with the approximate refractive indices $\alpha = 1.56$ and $\gamma = 1.57$. In parallel polarized light, nicols crossed: Birefringence is moderate, the colors being first order grays. Extinction is parallel and elongation negative. The grains are too minute for further measurements.

Vanillyl *n*-Nonoylamide.—Normal nonoic acid was purified by distillation. Condensed, through the acid chloride, with vanillyl amine, a yield of 76% of the theoretical equivalent of vanillyl *n*-nonoylamide was obtained. The substance crystallized slowly. Recrystallized from a mixture of ether and petroleum ether, it softened at 47° and was completely melted at 52° . It, therefore, still contained a small amount of impurities.

Calc. for $C_{17}H_{27}NO_8$: C, 69.6; H, 9.3; N, 4.77.

Found: C, 69.3; H, 9.1; N, 4.69.

Vanillyl *n*-nonoylamide is soluble in ether and in chloroform, and is slightly soluble in hot petroleum ether. It is an extremely pungent substance, being even more disagreeable to handle than vanillyl *n*-octoylamide. Its pungency to the taste is about the same as that of capsaicin.

Optical-crystallographic Data.—The optical properties of this substance are practically the same as those of vanilly *n*-octoylamide, so far as they could be observed, except for the refractive indices, which are: $\alpha = 1.57$ and $\gamma = 1.59$.

Vanillyl *n*-Decoylamide.—Capric acid (normal decoic acid) was prepared by fractionation of the methyl esters of the coconut oil fatty acids. The methyl ester boiling at $112-6^{\circ}$ under 15 mm. pressure was saponified and the acid recovered was crystallized and pressed out on filter paper in a cold room. The acid melted at $31-31.5^{\circ}$. A yield of 80% of vanillyl *n*-decoylamide was obtained. Recrystallized from petroleum ether, it melted at $59-60^{\circ}$.

> Calc. for $C_{16}H_{29}NO_{3}$: C, 70.3; H, 9.5; N, 4.55. Found: C, 70.1; H, 9.8; N, 4.58.

Vanillyl n-decoylamide is soluble in chloroform and in ether and is slightly soluble in boiling petroleum ether and in water. It is extremely pungent and the powdered substance causes coughing and sneezing.

Optical-crystallographic Data.—In ordinary light, vanillyl n-decoylamide is made up of splintery flakes and needles, the system being probably rhombic. Refractive indices: $\alpha = 1.545$, $\beta = 1.555$, $\gamma = 1.620$, $\gamma - \alpha =$ 0.075, all =0.005; β is usually seen lengthwise of the needles, and values intermediate between the other two indices crosswise. In parallel polarized light, nicols crossed: Birefringence is extremely strong, the colors being of upper first order, even on the thinner needles. Extinction is parallel and elongation usually negative, rarely positive. In convergent polarized light, nicols crossed: The crystals are too minute to yield good figures, but the class is biaxial, with the axial plane crosswise; 2E is small (calc. 23°) and the sign positive.

Vanillyl *n*-Undecoylamide.—An alcoholic solution of undecenoic acid, made by the dry distillation of castor oil, was hydrogenated, using

colloidal palladium as a catalyst. 96% of the theoretical amount of hydrogen was quickly absorbed. The undecoic acid obtained was used in the preparation of vanillyl *n*-undecoylamide, of which a yield of 80% was obtained. Recrystallized from petroleum ether containing 10% of ethyl ether, the substance melted at $54-6^\circ$.

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Calc. for C_{19}H_{\partial 1}NO_{\partial}: C, 71.0; H, 9.7; N, 4.35.
Found: C, 71.1; H, 10.0; N, 4.44.
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Vanillyl *n*-undecoylamide is insoluble in water, difficultly soluble in cold petroleum ether and easily soluble in ether.

The pungency of vanilly n-undecoylamide differs somewhat in character from that of the substances already described. The burning sensation is not so immediately apparent and affects the back of the tongue and the throat rather than the tip of the tongue.

Optical-crystallographic Data.—In ordinary light, vanillyl n-undecoylamide is in 4-sided or irregular plates, the system being apparently triclinic. Refractive indices: $\alpha = 1.515$, $\beta = 1.540$, $\gamma = 1.615$, $\gamma - \alpha = 0.100$, all ± 0.005 ; β is often obtained. In parallel polarized light, nicols crossed: Birefringence is extreme, the colors being of second order on even rather thin flakes. Extinction is inclined at varying angles, and elongation variable. In convergent polarized light, nicols crossed: Partial biaxial figures are frequently obtained, 2E being about 110° (calc. 106°) and the sign positive. Dispersion is distinct.

Vanillyl *n*-Dodecoylamide.—Lauric acid (normal dodecoic acid) was prepared by fractionating the methyl esters of coconut oil fatty acids. A yield of 70% of vanillyl *n*-dodecoylamide was obtained. It was recrystallized by pouring its ethereal solution into petroleum ether. It then melted at $60-1^{\circ}$ (corr.).

Calc. for $C_{20}H_{33}NO_3$: C, 71.6; H, 9.9; N, 4.17. Found: C, 71.2; H, 10.2; N, 4.26. Vanillyl *n*-dodecoylamide is insoluble in water but easily soluble in ether. In pungency it resembles vanillyl *n*-undecoylamide.

Optical-crystallographic Data.—In ordinary light, vanillyl n-dodecoylamide is in splintery plates, the system being apparently monoclinic. Refractive indices: $\alpha = 1.52$, $\beta = 1.54$, $\gamma = 1.60$, $\gamma - \alpha = 0.08$, all ± 0.01 . In parallel polarized light, nicols crossed: Birefringence is strong, the colors being 1st order yellow on even rather thin flakes. Extinction is inclined, reaching a maximum value of 30° , and elongation is negative. In convergent polarized light, nicols crossed: Rather indistinct figures are sometimes obtained, the class being biaxial, 2E moderate (calc. 100°) and sign positive.

Derivatives of the Acids of the Acrylic Acid Series.

Two derivatives of the acrylic acid series, to which the acid isolated from capsaicin belongs, have been made, namely, vanillyl crotonylamide and vanillyl undecenoylamide.

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Vanillyl Crotonylamide.—The chloride of crotonic acid was prepared from crotonic acid by the method described by Henry,¹ and was used in the preparation of vanillyl crotonylamide, of which a 50% yield was obtained. Recrystallized from boiling benzene, the substance melted at $119-20^{\circ}$ (corr.).

Calc. for $C_{12}H_{16}NO_8$: C, 65.1; H, 6.8; N, 6.33. Found: C, 64.9; H, 7.0; N, 6.25. Vanillyl crotonylamide is not easily soluble in ether or benzene but is quite soluble in chloroform and moderately soluble in water. It is slightly pungent.

Optical-crystallographic Data.—In ordinary light, vanillyl crotonylamide is in rods and irregular grains, the system being probably rhombic. Refractive indices: $\alpha = 1.515$, $\beta = 1.605$, $\gamma = 1.735$, $\gamma - \alpha = 0.220$, all ± 0.005 ; intermediate values are usually obtained. In parallel polarized light, nicols crossed: Birefringence is extreme, the strongest met with in the series studied, the colors being of high orders. Extinction is parallel, and elongation variable. In convergent polarized light, nicols crossed: Partial biaxial figures are occasionally obtained, 2E being extremely large, and the sign positive. Dispersion is distinct.

Vanillyl Undecenoylamide.—Undecenoic acid melting at 24.5° was obtained by the dry distillation of castor oil. Condensation with vanillyl amine gave a yield of 82% of vanillyl undecenoylamide. Purified by recrystallizing from petroleum ether, the substance melted at $53-5^{\circ}$ (corr.).

Calc. for C19H29NO3: C, 71.4; H, 9.1; N, 4.38. Found: C, 71.3; H, 9.3; N, 4.17.

Vanillyl undecenoylamide, like the corresponding saturated derivative, vanillyl undecoylamide, affects the throat rather than the tongue. Its powder is more irritating to the nose and throat, however, causing violent coughing and sneezing.

Optical-crystallographic Data.—In ordinary light, vanillyl undecenoylamide is in splintery masses and minute needles, the system being probably rhombic. Refractive indices: $\alpha = 1.55$, $\beta = 1.60$, $\gamma = 1.63$, $\gamma - \alpha =$ 0.08, all ± 0.01 . In parallel polarized light, nicols crossed: Birefringence is extremely strong, first to second order colors being shown on even minute needles. The extinction is parallel and the elongation negative. In convergent polarized light, nicols crossed: The needles are too minute to yield good figures; the class is biaxial, 2E extremely large and the sign negative.

Derivatives of Aromatic Acids.

Of the aromatic acids, the derivative of benzoic acid is the only one so far successfully prepared. One effort to prepare a cinnamic acid derivative resulted in a product without a sharp melting point which is, therefore, not described.

¹ Henry, Bull. acad. roy. belg., [3] 36, 42 (1898).

Vanillyl Benzoylamide.—Vanillyl benzoylamide was made by stirring a quantity of benzoyl chloride corresponding to one molecule with a quantity of vanillyl amine corresponding to two molecules, suspended in dry ether. It crystallized from alcohol in needles melting at 140-2°.

Calc. for C16H15NO8: C, 70.0; H, 5.9; N, 5.44. Found: C, 69.9; H, 6.0; N, 5.46.

Vanillyl benzoylamide is insoluble in ether but soluble in chloroform and alcohol. It is only moderately pungent.

Optical-crystallographic Data.—In ordinary light, vanillyl benzoylamide is in short rods and grains, the system being rhombic. Refractive indices: $\alpha = 1.590$, $\beta = 1.675$, $\gamma = 1.695$, $\gamma - \alpha = 0.105$, all ± 0.005 ; the individual indices are all frequently obtained. In parallel polarized light, nicols crossed: Birefringence is extreme, the colors being of high orders. Extinction is parallel, and elongation positive. In convergent polarized light, nicols crossed: Good biaxial interference figures are readily obtained, 2E being 85° (calc. 89°) and the sign negative. Dispersion is distinct.

Derivatives of *n*-valeric acid, of Wallach's "menthonensäure"¹ (a decenoic acid) and of Schneegans' decenoic acid² have been prepared, and were all found to be pungent substances. As none of them have crystallized, they cannot be described at present.

Pungency.

Capsaicin and the related substances described are practically devoid of odor and flavor.

The relative pungency of these substances was determined by ascertaining the minimum amount necessary to cause a distinct burning on the tip of the tongue.

It was found that 1/8000 mg. of capsaicin could be detected by this means, and comparisons were made with that amount of capsaicin as a standard. An alcoholic solution of capsaicin was prepared of such a concentration that one drop from a pipet giving 80 drops to the cc. contained the required amount. One drop was evaporated on a small microscopic cover glass and placed on the tongue, and the intensity of the sensation and its duration noted.

Alcoholic solutions of the substances to be tested were diluted until the residue of a drop from the same pipet gave, as nearly as could be determined, the same degree of pungency. It is self-evident that such a comparison can only be approximate. The tests, therefore, were repeated by several persons, in order to eliminate, so far as possible, the personal equation. The results are expressed on a percentage scale, the pungency

¹ Ann., **312**, 197 (1900). ² Ibid., **227**, 85 (1885).

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of capsaicin being taken as 100. The moderately pungent substances were not considered.

TABLE 1.—COMPARATIVE	PUNGENCIES.
Vanillyl <i>n</i> -hexoylamide	
Vanillyl <i>n</i> -heptoylamide	
Vanillyi <i>n</i> -octoylamide	
Vanillyl <i>n</i> -nonoylamide	100
Vanillyl <i>n</i> -decoylamide	50
Vanillyl <i>n</i> -undecoylamide	
Vanillyl <i>n</i> -dodecoylamide	
Vanillyl undecenoylamide	

This method was checked by the method of Pearson,¹ *i. e.*, by dilution until pungency was barely perceptible when a few drops of the solutions were tasted.

Zingerone,² (4 - hydroxy - 3 - methoxy - phenylethylmethyl ketone), CH₃O

HO— \bigcirc CH₂CH₂COCH₃, one of the pungent principles of ginger, is far less pungent than capsaicin. A direct test upon the tongue, as described above, as well as a test by Pearson's method, showed it to have approximately one-thousandth the pungency of capsaicin. Vanillyl acetamide, CH₃O

HO-CH₂NHCOCH₃, notwithstanding its structural similarity to zingerone, is not pungent.

The property of pungency would seem to be, to some extent, dependent upon solubility. Zingerone is sparingly soluble in water and easily soluble in most of the organic solvents, with the exception of petroleum ether. It thus corresponds with the more pungent of the vanillyl-acyl amides. Vanillyl acetamide, on the other hand, is quite soluble in water, but difficultly soluble in ether.

Backman³ shows that, in order for a substance to be odorous, it must be sufficiently soluble in both water and lipoids, since the cells of the nose are covered with a watery fluid, while they themselves ^{*}contain lipoid granules.

Durrans,⁴ in a valuable paper on the relationship between odor and chemical constitution, concludes that "a high molecular weight undoubtedly suppresses an odor, but a moderate molecular weight increases" it." The following table, given by Durrans, expresses this relation:

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<sup>1</sup> Pharm. J., 103, 78 (1919).
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² Nomura, J. Trans. Chem. Soc., 111, 769 (1917); Lapworth, et al., J. Trans. Chem. Soc., 111, 777, 790 (1917).

* J. physiol. path. gen., 17, 1 (1917).

* Perfumery Essent. Oil Record, 10, 104 (1919).

RELATION BETWEEN MOLECULAR WEIGHT AND INTENSITY OF ODOR.

	Odor develops.	Maximum odor.	Odor lost.
Aliphatic saturated alcohols	C ₅	C ₈	C14
Aliphatic saturated aldehydes	C1	C10	C16
Aliphatic saturated ketones	C ₈	C11	C16
Aliphatic saturated acids	C1	Съ	C14
Aliphatic saturated esters	C ₆	C ₈	C17

In the absence of a scientific method for the classification and measurement of odors, any attempt, such as the above, to correlate odor with chemical constitution must necessarily be largely empirical. It is, however, interesting to note that the increase in pungency to a maximum and subsequent decrease with increasing molecular weight would seem to run closely parallel with the variations of odor in series of organic substances brought out by Durrans.

Summary and Conclusions.

The condensation products of vanillyl amine with acetic, propionic, butyric, isobutyric, *n*-hexoic, *n*-heptoic, *n*-octoic, *n*-nonoic, *n*-decoic, *n*-undecoic, *n*-dodecoic, crotonic, undecenoic and benzoic acids have been prepared and described.

In the homologous series of the derivatives from saturated fatty acids, the solubility in water decreases with rising molecular weight, while the solubility in ether increases; whereas pungency increases until it reaches a maximum in vanillyl *n*-nonoylamide, then decreases or changes in character as the molecular weights increase.

Conclusions as to the effect of a double bond in the side chain cannot at present be drawn, as only two derivatives of the acrylic acid series have been prepared. Comparison of one of these (vanillyl undecenoylamide) with the corresponding saturated derivative, however, seems to indicate that the double bond may not increase the pungent taste but may increase the other irritating properties.

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