[Contribution from the Laboratory of Organic Chemistry of the University of Wisconsin]

The Constituents of the Volatile Oil of Catnip. I. Nepetalic Acid, Nepetalactone and Related Compounds

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The common catnip plant, *Nepeta Cataria*, indigenous to Europe but now naturalized and widely distributed throughout the United States, contains about 0.3% of a volatile oil. This oil carries the characteristic odor of the plant and generally is obtained from the whole fresh plant by distillation with steam. Although some earlier work had been done on the chemical nature of this oil, it was Kremers[3] who first found about 85% of the oil to be soluble in an aqueous sodium hydroxide solution; acidification of the resulting alkaline solution precipitated an acid as a viscous oil that slowly crystallized on standing. The acidic material prepared in this manner is practically odorless. The characteristic catnip odor which is so attractive to many species of the cat family, remains in the relatively small (about 15%) neutral portion of the oil.

An investigation of the chemical nature of the acidic fraction of the oil of catnip has been made by Meyer.[4] She studied the crystalline acid, m. p. 71–72°, obtained from the acidic fraction, and from molecular weight determinations together with analyses of the acid and a number of its salts and solid esters, assigned to it the formula, $C_{10}H_{16}O_3$. It was found to be optically active, $\alpha^{24}D$ +38°36′ for a freshly prepared absolute alcohol solution; this value changed to +36°28′ after two days and to +5° after three months. The acid showed a carbonyl function that gave derivatives with sodium bisulfite, hydroxylamine and semicarbazide; however, it did not reduce Fehling solution. In some experiments it was possible to obtain a positive iodoform reaction, but in other attempts this reaction was obtained with difficulty. Reaction with acetyl chloride and acetic anhydride indicated the presence of an ester-forming hydroxyl group, but no definite acetyl derivative was isolated. Meyer carried out a series of oxidation experiments using both chromic acid and permanganate as oxidizing agents at various temperatures, and reported the isolation of a number of acidic oxidation products among which were acetic acid and two solid acids that melted at 85 and 250°; the neutral equivalents of the solid acids were found to be 103 and 155, respectively. Carbon and hydrogen analyses and the molecular weight of the acid, m. p. 85°, indicated that it had the molecular formula $C_{11}H_{16}O_4$. No further identification of these acids was made.

The present paper is the first report of a further study[5] of the various constituents of the oil of catnip and deals specifically with the structure of the acidic component for which the name *nepetalic acid* is proposed. Meyer's molecular formula, $C_{10}H_{16}O_3$, has been confirmed and for this solid acid the structure I is proposed. In solution, however, the aldehydo-acid structure I appears to exist in two tautomeric forms, the enolized structure II, and the hydroxy lactone structure III. The exact structure of the C_5H_7 grouping has not been determined but it is believed to be a trisubstituted cyclopentane nucleus. The main line of evidence for structure I is based on the oxidative degradation of nepetalic acid. Alkaline hydrogen peroxide converts this acid, probably as form II, into formic acid and a liquid keto-acid IV for which the name, *nepetonic acid*, is proposed. These acids were isolated from the oxidation reaction in yields of 30% and 67% of the theoretical, respectively. Nepetonic acid when treated with a five molar excess[6] of sodium hypoiodite gives an 85% yield of iodoform and an 80% yield of the dibasic acid, $C_8H_{12}O_4$, m. p. 117–118°, to which the name, *nepetic acid*, is assigned. Its unusual stability together with the fact that it contains one C-methyl group leads to the conclusion that nepetic acid is a methyl-dicarboxy-cyclopentane (V). This acid distils unchanged at 168–170° (0.1 mm.), but acetic anhydride converts it to an anhydride (Va) which yields the original acid on

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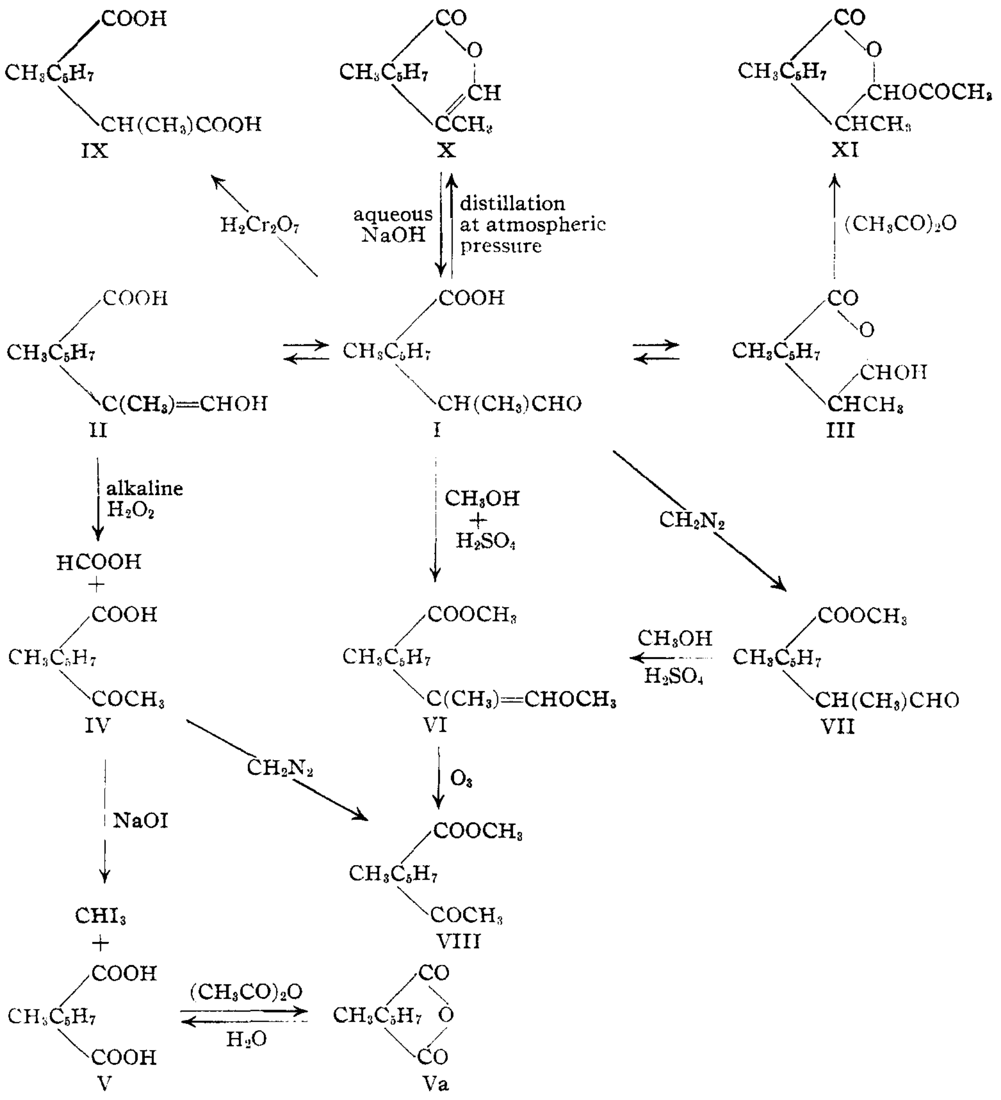
[3] Unpublished work of Dr. Edward Kremers, now Emeritus Professor of Pharmaceutical Chemistry in the University of Wisconsin.

[4] Minnie Meyer, Ph.D. Thesis, University of Wisconsin, 1936; *Pharm. Arch.*, **7**, 17–52 (1936). This work was done under the direction of Professor Kremers.

[5] This work was undertaken in February, 1940, at the suggestion of Professor Kremers, who, since his retirement in 1935, has not been able to continue his study of the problem.

[6] Such an excess of sodium hypoiodite seems necessary to produce the maximum yield of iodoform; a single molar equivalent gives only a 10% yield. Levulinic acid shows a similar behavior toward this reagent.



hydrolysis. This latter fact together with the space requirements of the bicyclic structures III and X indicates that the carboxyl groups of nepetic acid are in the *cis* position. These groups may be in either the 1,2 or 1,3 positions of the cyclopentane ring since anhydrides of both types are known[7] and space models show that structures III and X may be formed from either of these positions, even though the 1,3 linkage would require a seven-membered ring in the bicyclic structures. Work which is expected to establish the relative positions of the substituent groups in nepetic acid (V), nepetonic acid (IV), and nepetalic acid (I) is now in progress.

While the oxidations outlined above point to I as the structure of nepetalic acid, other data which have been collected in the present work confirm this conclusion. Meyer's observation that nepetalic acid does not reduce Fehling solution is valid when the test is carried out in the usual way; however, if the Fehling solution is diluted with two volumes of water and this diluted solution warmed to about 60°, addition of nepetalic acid produces the characteristic cuprous oxide precipitate. The acid reduces Tollens solution readily. It generally has been impossible in the present work to obtain a characteristic iodoform test with nepetalic acid. It is likely that in those cases when Meyer obtained an indication of this latter reaction the hypoiodite oxidized some of the nepetalic acid (form II) to a small amount of nepetonic acid (IV) which, of course, would give the

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(7) Perkin, *J. Chem. Soc.*, **65**, 588 (1894); Pospischill, *Ber.*, **31**, 1953 (1898).

reaction. Both I and IV react quantitatively with one equivalent of diazomethane to give esters VII and VIII. All of the carbonyl compounds I, IV, VII and VIII form characteristic semicarbazones. The structure of the unsaturated ether-ester VI which may be made from both I and VII is indicated by its conversion by ozone into the ester VIII which also may be prepared from nepetonic acid (IV). The dimethyl nepetalate (VI) shows no carbonyl function; it adds bromine rapidly without the evolution of the hydrogen bromide that is always formed when either I or VII is forced into reaction with bromine. The dibasic acid IX undoubtedly represents the structure of the acid, m. p. 85°, neut. equiv. 103, that Meyer[4] obtained from the oxidation of nepetalic acid with chromic acid. It is now suggested that IX be called *nepetalinic acid.*

The unsaturated lactone X, for which the name, *nepetalactone*, is proposed, is a limpid liquid with a mint-like odor that boils at 71–72° (0.05 mm.). Its formation from nepetalic acid by heat indicates either structure II or III as its immediate precursor. This lactone has no carbonyl function, is insoluble in cold aqueous sodium bicarbonate solution, but does dissolve with considerable evolution of heat when shaken with 10% aqueous sodium hydroxide. It readily adds one equivalent of bromine. In the early part of the present work this lactone proved to be a useful intermediate in the purification of nepetalic acid (I). The precipitation of this acid from an aqueous alkaline extract of oil of catnip generally gave an oil that crystallized very slowly if at all. If such an oil were converted to the lactone X, and this lactone, after redistillation, reconverted to I by solution in 10% aqueous alkali followed by immediate acidification, there was obtained a viscous, amorphous precipitate that generally crystallized better than the nepetalic acid that had been obtained directly from the oil of catnip by alkali extraction. After it was known that the carbonyl function of I was in the form of an aldehyde it was found that extraction of the oil of catnip with a saturated sodium bicarbonate solution gave an extract that yielded a crystalline form of I on acidification. However, only about 30% of the oil dissolved in this reagent as compared to the 85% that went into solution in 10% aqueous sodium hydroxide. The oil left after the bicarbonate extraction reacted with aqueous sodium hydroxide, as does the lactone (X), with the evolution of considerable heat, and about 55% of the original amount of oil passed into the alkali solution. This behavior suggests that a considerable amount of the nepetalic acid that is obtained from the oil by extraction with aqueous sodium hydroxide comes from the saponification of nepetalactone in the oil. This conclusion was confirmed by distillation of the oil remaining after the bicarbonate extraction; approximately 45% of the weight of original oil was collected as the lactone (X). The presence of both I and X in the oil of catnip was shown by distillation of the untreated oil. About 50% of the oil distilled as the lactone, 33% as nepetalic acid, b. p. 136–138° (0.1 mm.), and 14% as a viscous, yellow, neutral fraction, b. p. 210–214° (0.1 mm.), that possesses the characteristic odor of the catnip oil. The chemical nature of this neutral constituent of the oil will be the subject of a later report. From these facts it seems quite probable that the nepetalic acid which is extracted from the original oil by the aqueous sodium bicarbonate was formed by hydrolysis of the nepetalactone during the steam distillation of the oil from the plant.

The acetate (XI), m. p. 68–69°, is quantitatively formed by the action of acetic anhydride on nepetalic acid. The fact that this acetate is insoluble in dilute alkali and does not decolorize bromine in carbon tetrachloride indicates that it is derived from the hydroxy-lactone form (III) of nepetalic acid.

Experimental

All α_D herein reported were calculated from rotations determined in chloroform solution in a 22-cm. tube.

Nepetalic Acid (I).—At the start of this work nepetalic acid, which had been prepared and left by Meyer in the Laboratories of the School of Pharmacy of the University of Wisconsin, was used. The authors wish to express their appreciation of Professor Kremers' kindness in making available this material to them. This acid, which had been obtained from oil distilled from plants grown in 1934 and 1935, had changed, after standing since 1936, from a solid to a slushy mixture of oil and solid. The solid was removed from this slush by solution of the oily portion in a mixture of ether and petroleum ether. A 24-g. sample of the oil–solid mixture after stirring with a mixture of 60 ml. of petroleum ether, b. p. 40–60°, and 7 ml. of diethyl ether left 11.6 g. of the solid acid which, after recrystallization from an ether–petroleum ether mixture, melted at 75–76°. Meyer[4] reported the melting point of this acid as 71–72°.

Most of the work which is reported here was done with nepetalic acid extracted from oil of catnip purchased from Fritzsche Brothers, Inc., New York. This oil was steam distilled from the 1939 summer crop grown in Michigan. A 26-g. sample of the oil was extracted by shaking with 65 ml. of a 10% aqueous solution of sodium hydroxide. As noted by Meyer, 85–90% of the oil went into the water layer with the evolution of sufficient heat to bring the temperature of the extraction mixture to about 60°. After cooling, the aqueous layer was extracted with three 25-ml. portions of ether. The combined ether extracts on evaporation were found to contain 2.8 g. (11%) of the neutral portion of the oil. Acidification of the alkaline solution to congo red precipitated an oil which could not be caused to crystallize under the aqueous layer. The oil was taken up in ether and this solution dried over drierite. Evaporation of the ether left 23 g. of an oil that crystallized very slowly and then only partially. This crystallization could be improved both as to rate and quantity by seeding the oil with a crystal of nepetalic acid. The solid acid from this extract melted at 75–76° and was identical with that obtained above from the 1934 and 1935 oils.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.17; H, 8.76. Found: C, 65.13; H, 8.87; carbon-methyl determination[8] showed 1.96 C-CH_3 groups.

Meyer[4] reported the preparation of a bisulfite addition compound of nepetalic acid. It was found in the work now reported that this compound, m. p. 95–97°, can be prepared in 65% yield from the acid by warming the latter on a steam-bath for ten minutes with a 30% solution of sodium bisulfite. The crystalline acid may be regenerated from the bisulfite addition compound by treatment with 5% sulfuric acid. Since the yield of recovered acid from this operation amounted to only 60% of the theoretical, the bisulfite procedure does not offer a very satisfactory purification route.

The most satisfactory method of preparing the crystalline nepetalic acid starts with the extraction of oil of catnip with a saturated aqueous sodium bicarbonate solution. About 30% of the oil goes into the bicarbonate solution with a vigorous evolution of carbon dioxide. Acidification of the resulting aqueous solution precipitates the nepetalic acid as a mixture of oil and solid which crystallizes further on standing. The nepetalic acid prepared in this manner melts at 74–75°; $\alpha^{23}D$ +48.1°. This is a considerably higher rotation than that obtained with nepetalic acid extracted from oil of catnip with aqueous sodium hydroxide and suggests that this latter reagent causes some racemization of the acid.

Nepetalic acid may also be prepared from the nepetalactone as described below.

Nepetalic acid gave no significant amount of iodoform when treated with five-fold excess of an alkaline solution of sodium hypoiodite. With Tollens solution a silver mirror formed rapidly. When the ordinary Fehling solution was diluted with two volumes of water and then warmed to 60°, addition of the acid produced an immediate precipitate of cuprous oxide.

Nepetalic acid semicarbazone was prepared by treating an aqueous-alcoholic solution of nepetalic acid with an aqueous solution of semicarbazide hydrochloride buffered with sodium acetate. This derivative melted at 160–161°.

Anal. Calcd. for $C_{11}H_{19}O_3N_3$: C, 54.78; H, 7.94. Found: C, 54.61; H, 8.17.

Methyl Nepetalate (VII).—Nepetalic acid (6.3 g.) was treated with an ether solution of diazomethane until a slight excess of one equivalent had been added. At this point a permanent yellow color remained in the ether solution. Evaporation of the ether and distillation of the remaining oil gave a product that boiled at 113–115° (12 mm.); $n^{25}D$ 1.4555; $\alpha^{23}D$ +16.1°. The yield was practically quantitative.

Anal. Calcd. for $C_{11}H_{18}O_3$: CH_3O, 15.65. Found: CH_3O, 15.85.

This ester yields a semicarbazone that melts, after recrystallization from methanol, at 150–151°.

Anal. Calcd. for $C_{12}H_{21}O_3N_3$: C, 56.48; H, 8.28 Found: C, 56.16; H, 8.47.

Dimethyl Nepetalate (VI).—A solution of 2 g. of nepetalic acid in 10 ml. of methanol containing three drops of concentrated sulfuric acid was refluxed for six hours. After this time the mixture was poured into water and extracted with ether. The ether extract was washed with water and sodium bicarbonate solution and then dried. After removal of the ether the remaining oil distilled at 128–131° (12 mm.); $n^{25}D$ 1.4548; $\alpha^{25}D$ +10.8°.

Anal. Calcd. for $C_{12}H_{20}O_3$: CH_3O, 29.2. Found: CH_3O, 29.8.

Methyl nepetalate (VII) could be converted into VI by refluxing a methanol solution of the monomethyl ester that contained a few drops of concentrated sulfuric acid. The di-ester so obtained had a methoxyl content of 32.2% which indicated that it contained some of the trimethyl derivative, *i. e.*, the dimethyl acetal of VII, the methoxyl content of which is 38.1%.

The dimethyl ester VI had a saponification equivalent of 215, gave no reaction with semicarbazide, and rapidly added bromine in a carbon tetrachloride solution without the liberation of hydrogen bromide.

Ozonolysis of Dimethyl Nepetalate (VI). Methyl Nepetonate (VIII).—A solution of 3.25 g. of VI in 40 ml. of ethyl bromide was treated with ozonized oxygen for two and one-half hours. The solution was then transferred to a separatory funnel and the solvent removed under diminished pressure. The remaining oily material was decomposed in the apparatus recommended by Church and Whitmore.[9] The hydrolysis mixture was warmed slowly to boiling and then steam distilled. The distillate was extracted with 10 ml. of ether and the extract dried. Upon evaporation of the solvent 0.95 g. of methyl nepetonate (VIII) boiling at 64–66° (0.4 mm.), $n^{25}D$ 1.4502 was obtained. This ester absorbs bromine in carbon tetrachloride solution with the elimination of hydrogen bromide and reacts with sodium hypoiodite to give iodoform. It contained 16.75% methoxyl (calcd., 16.85%). It yielded a semicarbazone, m. p. 180–181°, which was identical with that obtained from the ester resulting from the action of diazomethane on nepetonic acid (IV).

Anal. (of semicarbazone). Calcd. for $C_{11}H_{19}O_3N_3$: C, 54.77; H, 7.88; CH_3O, 12.85. Found: C, 54.41; H, 8.09; CH_3O, 12.68.

Nepetalactone (X). (a) From Nepetalic Acid.—The viscous oil obtained from the acidification of the sodium hydroxide extract of oil of catnip was slowly distilled at

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[8] Kuhn and Roth, *Ber.*, **66**, 1274 (1933).

[9] Church and Whitmore, THIS JOURNAL, **54**, 3710 (1932).

atmospheric pressure. It yielded an oil and a quantity of water approximately equivalent to the loss of one mole of water per mole of nepetalic acid. The oil was taken up in ether and, after drying and removal of the ether, redistilled. It boiled at 71–72° (0.05 mm.); $n^{25}\text{D}$ 1.4859; $d^{25}{}_4$ 1.0663; $\alpha^{23}\text{D}$ +3.6°. This lactone adds one equivalent of bromine in carbon tetrachloride solution. Further absorption of bromine is accompanied by the evolution of hydrogen bromide. The same product was obtained by the dehydration of the crystalline nepetalic acid that was precipitated from the sodium bicarbonate extract.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.25; H, 8.49. Found: C, 72.01; H, 8.66.

(b) **From Oil of Catnip.**—The nepetalic acid was removed from a 5.5-g. sample of oil of catnip by shaking the oil with 200 ml. of a saturated aqueous solution of sodium bicarbonate. The remaining insoluble oil was taken up in ether, and after drying, the ethereal solution was fractionated. The first fraction to come over after the removal of the ether was nepetalactone, b. p. 71–72° (0.05 mm.), and it amounted to 2.4 g. or 45% of the oil originally taken.

Nepetalactone also could be distilled out of the untreated oil of catnip. A 18.4-g. sample was fractionated under diminished pressure and yielded 9.5 g. of lactone, b. p. 71–85° (0.05 mm.), 6.0 g. of nepetalic acid, b. p. 135–140° (0.05 mm.) and 2.6 g. of a yellow, viscous oil, b. p. 210–214° (0.05 mm.). Redistillation of the low boiling fraction yielded the lactone, b. p. 71–72° (0.05 mm.); $\alpha^{23}\text{D}$ −13.0°. The difference between the rotation of this lactone and the one prepared from nepetalic acid that had been extracted from the oil with alkali is probably due to partial racemization during the extraction.

Nepetalic Acid from Nepetalactone.—The lactone dissolved, with the evolution of considerable heat, to a clear solution when shaken with an excess of a 10% solution of sodium hydroxide. The alkaline solution was acidified and the precipitated acid was taken up in ether and the ethereal solution dried over anhydrous sodium sulfate. After evaporation of the ether under diminished pressure, petroleum ether (b. p. 40–60°) was added to the residue and the undissolved oil frozen by dry-ice. The petroleum ether layer was decanted, and after warming up to room temperature, the oil was again treated with petroleum ether and allowed to stand at room temperature. Crystals slowly formed in the oil and, after no more appeared to form, the crystals were recrystallized from an ether–petroleum ether solution. About one-third of the weight of the lactone was obtained as crystalline nepetalic acid, m. p. 71–72°.

Nepetonic Acid (IV).—A solution of 17 g. of nepetalactone (or an equivalent amount of crystalline nepetalic acid) in 190 ml. of 5% sodium hydroxide was treated with 75 ml. of 30% hydrogen peroxide ("Superoxol"). Within a few minutes the reaction mixture became warm and it was necessary to cool it in cold water to prevent frothing. After standing for several hours the solution was acidified with dilute sulfuric acid, saturated with sodium chloride and extracted with 150 ml. of ether. The dried ethereal solution was distilled and 2.4 g. of material boiling below 110° together with 11.7 g. (67%) of nepetonic acid, b. p. 119–120° (0.2 mm.) were obtained. The low boiling material on fractionation gave 1.5 g. (30%) of formic acid, b. p. 100–102°; *p*-bromophenacyl ester, m. p. 141–142° (no depression when mixed with an authentic specimen). Other properties of nepetonic acid are, $n^{25}\text{D}$ 1.4681; $d^{25}{}_4$ 1.1014; $\alpha^{23}\text{D}$ −7.9°; neut. equiv., 170 (calcd. 170).

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.49; H, 8.29. Found: C, 63.12; H, 8.40.

Nepetonic Acid Semicarbazone was prepared in the usual way and found to melt, after several recrystallizations from ethyl alcohol, at 168–169°.

Anal. Calcd. for $C_{10}H_{17}O_3N_3$: C, 52.95; H, 7.73. Found: C, 52.87; H, 7.61.

Nepetic Acid (V).—To 24.6 g. of nepetonic acid dissolved in 1.5 liters of 10% sodium hydroxide was added a solution of 300 g. of iodine and 600 g. of potassium iodide in 2.4 liters of water. After stirring for three hours the precipitated iodoform was filtered off and dried. It weighed 48 g. (85%). The filtrate was treated with a saturated solution of sodium bisulfite and sufficient concentrated hydrochloric acid to destroy the hypoiodite and to leave the solution basic to congo red. The solution then was evaporated to 2.2 liters cooled, acidified to congo red and extracted with 1.5 liters of ether in eight portions. The ether extracts were combined, washed with 25 ml. of dilute sulfurous acid, dried over anhydrous sodium sulfate and distilled. A yield of 18.9 g. of nepetic acid boiling at 168–170° (0.1 mm.) was obtained. An additional 1.4 g. of the acid was obtained by evaporating the aqueous layer to 600 ml. (removing the inorganic salts from time to time by cooling and filtering), extracting with six 150-ml. portions of ether, drying and evaporating the ether. The total yield of the nepetic acid was 20.3 g. (81%). Recrystallization of this acid from an ether–petroleum ether mixture gave white crystals, m. p. 117–118°. Nepetic acid is quite soluble in water and, with the exception of petroleum ether, the common organic solvents. Its neut. equiv. was found to be 85 (calcd. 86); $\alpha^{23}\text{D}$ −35.4°.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.78; H, 7.03. Found: C, 55.73; H, 7.21. Carbon-methyl determinations[8] showed 0.96 C-CH_3 group in nepetic acid.

Nepetic Anhydride (Va).—Two grams of nepetic acid was refluxed for 2.5 hr. with 25 ml. of acetic anhydride after which time the excess acetic anhydride was removed by distillation. The remaining residue of nepetic anhydride was an oil that boiled at 98–99° (0.5 mm.); $n^{25}\text{D}$ 1.4744; $d^{25}{}_4$ 1.1601; $\alpha^{23}\text{D}$ +22.8°. This oil readily went into solution in dilute alkali. Acidification of this alkaline solution and extraction with ether gave the original nepetic acid, m. p. 117–118°.

Anal. Calcd. for $C_8H_{10}O_3$: C, 62.30; H, 6.55. Found: C, 62.61; H, 6.73.

Nepetalinic Acid (IX).[10]—To a solution of 28 g. of potassium dichromate in 60 ml. of water was added 10 g. of finely powdered nepetalic acid and to this mixture 40 ml. of concentrated sulfuric acid was slowly added with constant shaking. The reaction mixture became quite warm and was cooled. When the heat of the reaction subsided the resulting solution was heated on a steam-bath for two hours. After this time the solution was poured into 100

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[10] This experiment and the analysis of the resulting acid were carried out by Meyer; the above procedure is taken from her report, ref. 4.

ml. of water, whereupon a pasty mass, that solidified on standing, separated. This precipitate was warmed on a steam-bath with 80 ml. of 5% sulfuric acid and after cooling the insoluble crystalline acid filtered off. This acid was dissolved in 80 ml. of 5% sodium hydroxide solution, filtered, and the filtrate poured into 150 ml. of a 10% sulfuric acid solution. The acid slowly crystallized from this aqueous acid solution and was filtered off in several crops. Repetition of this solution in alkali and reprecipitation by sulfuric acid gave an acid that melted at 85–86°; neut. equiv., 103; mol. wt. (in camphor), 200 (calcd. 200).

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.00; H, 8.00. Found: C, 59.81; H, 8.07.

Nepetalic Acid Acetate (XI).—A mixture of 1 g. of nepetalic acid, m. p. 74–75°, and 1.2 g. of acetic anhydride was heated for four hours at 100° and then fractionally distilled. After the acetic acid and unchanged anhydride were removed, the nepetalic acid acetate distilled at 124–126° (0.1 mm.). It solidified in the receiver. After recrystallization from an ether–petroleum ether mixture it melted at 68–69°; $\alpha^{23}D$ +72.2°. The yield was practically quantitative. This acetate is insoluble in aqueous sodium hydroxide and shows no reaction with bromine in carbon tetrachloride.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.69; H, 8.01. Found: C, 63.61; H, 8.21.

Summary

The acidic constituent of the volatile oil of catnip, to which the name nepetalic acid is assigned, is found to be a tri-substituted cyclopentane with —CH_3, —COOH and —$CH(CH_3)CHO$ as the substituent groups. This aldehydo-acid appears to have two tautomeric forms (a) an enol form in which the aldehyde-containing substituent exists as —$C(CH_3)$=CHOH, and (b) a bicyclic hydroxylactone that yields a neutral acetate with acetic anhydride.

Distillation at atmospheric pressure converts nepetalic acid into an unsaturated lactone, nepetalactone, a compound which is found to make up about half of the oil of catnip. This lactone is rapidly saponified and taken into solution by aqueous sodium hydroxide and together with nepetalic acid comprises the 85% of the oil that dissolves in this solvent.

Nepetalic acid is oxidized by hydrogen peroxide in alkaline solution to formic and nepetonic acids. The latter acid contains an acetyl group in the place of the —$CH(CH_3)CHO$ substituent of nepetalic acid. Sodium hypoiodite converts nepetonic acid into nepetic acid, a methyldicarboxycyclopentane. Oxidation of nepetalic acid with chromic acid converts the aldehyde group to a carboxyl and produces the dibasic nepetalinic acid. A number of derivatives of these various acids are described.

MADISON, WISCONSIN RECEIVED MARCH 8, 1941

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Selective Hydrogenation of Derivatives of Pyrrole, Indole, Carbazole and Acridine

BY HOMER ADKINS AND HARRY L. COONRADT

The phenylpyrroles, indoles, carbazoles and acridines offer many possibilities for partial and selective hydrogenation. The yield of compounds produced is determined by the catalyst and other conditions of reaction as well as by the structure of the particular hydrogen acceptor involved. This paper presents the experimental results obtained in the partial and complete hydrogenation of twenty-one heterocyclic compounds over copper chromite and Raney nickel. An attempt has been made to correlate the behavior of these compounds toward hydrogenation with their electronic structure.

The pyrrole nucleus requires more drastic conditions for hydrogenation than does the benzenoid nucleus. However substitution of a carbethoxy group on the nitrogen of pyrrole so decreases resonance that the ring may be hydrogenated under very mild conditions.[1,2] The phenyl group has a somewhat similar effect for 1-phenylpyrrole was converted under mild conditions to 1-phenylpyrrolidine over Raney nickel.[1] However either a carbethoxy or a phenyl group in the 2-position is very much less effective in decreasing ring resonance than when it is in the 1-position. 2-Phenylpyrrole I underwent hydrogenation in both rings over nickel at 165°, 27% 2-cyclohexylpyrrolidine (II), 15% 2-phenylpyrrolidine (III), and 40% unchanged 2-phenylpyrrole being isolated after a typical two-hour run. Nickel was there-

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[1] Signaigo and Adkins, THIS JOURNAL, **58**, 709 (1936).

[2] Rainey and Adkins, *ibid.*, **61**, 1104 (1939).