Anal. Calcd. for $C_{12}H_{15}Br_3$: Br, 60.09. Found: Br, 59.70, 59.74.

Sixteen cc. of concentrated sulfuric acid and 19 cc. of fuming nitric acid (d. 1.50) were mixed and placed in a 50-cc. flask attached to a reflux condenser with a ground glass joint. The mixed acids were cooled in an ice-bath and 4 cc. of hydrocarbon added slowly. The reaction was completed by refluxing gently for fifteen minutes. After cooling, the mixture was poured into cold water and the precipitated nitro-compound filtered off. It was washed and dried: crude yield 6 g.; m. p. 111.5–112°. The product was recrystallized from absolute alcohol, then from a dioxane–water mixture, and finally from absolute alcohol; m. p. 112.4–112.6°. The recorded melting point is 108–109°.

Anal. Calcd. for $C_{12}H_{15}N_3O_6$: N_2, 14.16. Found: N_2, 14.15, 14.24.

Summary

Methods are described for the preparation of mesitylene by condensing methyl alcohol with toluene or *m*-xylene in the presence of aluminum chloride and for the preparation of symmetrical triethylbenzene from ethyl alcohol and benzene.

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[CONTRIBUTION FROM THE LABORATORIES OF ARTHUR D. LITTLE, INC.]

A New Substance, Cativic Acid, and its Preparation, Properties and Derivatives

BY NICHOLAS L. KALMAN

The "Cativa" tree, *Prioria copaifera*, Griseb.,[1] is found extensively in the lowlands bordering the Caribbean Sea from Mexico into Colombia, the trees reaching a diameter up to 5 ft. (1.5 meters) and a height of 100 ft. (30 meters). It yields a copious oleo-resinous exudate about which very little has been learned until recently. Fawcett[2] reported that this substance, resembling copaiba balsam, was soluble in many organic solvents, insoluble in water, reacted with aqueous and fused alkalies and gave 90% of a wide-boiling product on destructive distillation. Dirmitt,[3] after noting the involatility of the exudate, found hydrocarbons in the cracked distillate, and, by analysis, the formula $C_{24}H_{40}O_2$. Umney[4] reported some properties and that the exudate (now called "Cativo") was chiefly an acid resin. Weigel[5] pronounced the substance to be a "resinol-acid resin," observed the same characteristics as Umney and reported 75–80% resin acids, 13% unsaponifiable, 2% essential oil and 3% water and foreign matter.

Experimental

Preliminary Examination.—Investigation of Cativo samples from different places and taken at different times of year indicated a fairly uniform composition, the exudate being very sticky, viscous, with a cold flow and a muddy brown color due to fine suspended matter. When this is removed and the 0.5% of water evaporated, the product is clear and transparent. The cativo is insoluble in water, contains less than 2% of volatile oil and no free or esterified benzoic or salicylic acid. Over 95% appears to consist of a high boiling cyclic acid and its ester with the corresponding alcohol, which classifies cativo as a resin. Previous observations[4,5] were confirmed: (averages) acid no., 149.5; sap. no., 169.2; ester no., 19.7. There was also found 0.4% of an acid extractable from the ethereal solution with sodium bicarbonate; acid no., 373.6.

Separation of Cativic Acid.—A filtered solution of cativo in petroleum ether was first shaken out with sodium bicarbonate, then carefully neutralized with 0.5 *N* alcoholic potassium hydroxide, and diluted with water until the alcohol content was 50%. The aqueous–alcoholic layer was then separated, and washed several times with petroleum ether. An excess of hydrochloric acid precipitated the acid, which was dissolved in petroleum ether, dried with calcium chloride, the solvent distilled and the residue dried at 100° at a 1-mm. pressure, to a brown, viscous, tacky semi-solid. To this acid we have given the name "Cativic acid."

Vacuum distillation results in decomposition of the cativic acid, unless the pressure is reduced to 5 mm. or less. At 1 mm. it comes over as an odorless, water-white, viscous liquid at 194–195°. Crystallization could not be induced, even by fractional vacuum distillation (20 fractions), decomposition of the purified salts or from aqueous alcohol or acetone.

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.36; H, 11.19; acid no., 183.2; mol. wt., 306. Found: C, 78.41; H, 11.06; acid no., 182.2; mol. wt. (f. p. of camphor), 296. Calcd. for $Al(C_{20}H_{33}O_2)_3$: Al, 2.98. Found: Al, 2.86.

The Ester, Cativyl Cativate.—The residual acid-free petroleum ether solution of cativo is washed several times with 50% aqueous alcohol, dried with calcium chloride, and the petroleum ether distilled off. Vacuum distillation of the residue in a nitrogen atmosphere at about 5 mm. removes a volatile oil below 100°, but the pleasant smelling, mobile residue will not distil even at 250°. Hydroly-

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[1] Griesebach, "Flora of the British West Indies."

[2] Wm. Fawcett, *Bull. Bot. Dept., Jamaica*, N. S., **4**, 77–78 (1897).

[3] Charles W. Dirmitt, "Contribution from the Chemical Laboratory of the Philadelphia College of Pharmacy, No. 172," *Am. J. Pharm.*, **70**, 10–18 (1898).

[4] E. M. Holmes, *Pharm. J.*, [4] **15**, 296 (1902).

[5] G. Weigel, *Pharm. Zentralhalle*, **44**, 147–150 (1903).

sis of the residue with alcoholic potassium hydroxide and separation of the products in the usual manner shows cativic acid to be the acid component. The alcohol component is a colorless, fairly viscous liquid, b. p. 208.5–209.5° at 4.5 mm. (uncorr.) with slight decomposition.

Anal. Calcd. for $C_{20}H_{36}O$: C, 82.12; H, 12.42. Found: C, 82.07; H, 11.94.

The acetate was prepared, b. p., with slight dec., 191° (2.5 mm.), a colorless, odorless, limpid liquid.

Anal. Calcd. for $C_{22}H_{38}O_2$: C, 78.97; H, 11.46; ester no., 167.8. Found: C, 79.13; H, 10.91; ester no., 161.3.

The alcohol seems to be that corresponding to the acid in the ester, and we have named it cativyl alcohol. We have here another example, frequent with plant exudates, of an acid esterified with the corresponding alcohol. The ester number of the original ester is 101.4; calcd. for cativyl cativate, 96.6.

Preparation and Properties of Cativic Acid

In addition to the above extraction method, cativic acid may be separated from cativo by (1) alcohol extraction and (2) fractional distillation. In the first method, cativo is triturated with 6 times its weight of 75% alcohol and allowed to settle. The cativic acid dissolves into the slightly greenish alcohol solution, while the sludge consists of the ester, ethereal oil and coloring matter. The alcohol may be substantially decolorized by sunlight or by a small amount of sodium hydrosulfite. The acid may be separated from the alcohol solution by extracting with petroleum ether or by diluting to 50% alcohol content, which precipitates it. In the second method, vacuum distillation is begun with a pressure of 120–250 mm., the water, essential oil and traces of low-boiling acids passing off below 100° with a minimum of frothing, the vacuum being increased toward the end to hasten the separation. The pressure is now reduced to 1 mm. and the cativic acid distils at 194° (1 mm.), the yield being about 71% with 24.5% of undistillable ester. The low pressure is necessary to minimize decomposition; oxidation (especially rapid in the presence of the related hydrocarbon "cativene" which is obtained by the high temperature decarboxylation of cativic acid) is reduced in the presence of a nitrogen atmosphere, and the addition of aluminum foil prevents discoloration.

Properties.—Cativic acid as prepared by vacuum distillation shows sp. gr. 0.9987 at 23° and refractive index 1.5090 at 24°. It is insoluble in water and in 50% alcohol, but soluble in 75 and 95% alcohol, methanol, butanol, acetone, methyl ethyl ketone, ethyl and butyl acetates, ether, aromatic and petroleum hydrocarbons, chlorinated hydrocarbons, turpentine and other thinners, "Varnolene," oils, etc.

The "hot saponification" number of cativic acid, as with rosin acids, is several points higher than the "cold neutralization" number; therefore, the acid number is actually higher and the ester number lower than shown by analysis of cativo resin. The iodine number is variable, depending on test conditions:

Sample, g.	0.2287	0.3570	0.6465	0.1332	0.1787	0.3002
Time, hours	1	1	1	17	17	17
Iodine no.	107.0	85.0	50.6	164.9	146.2	102.8

Cativic acid resembles the rosin acids in certain chemical and physical properties, but differs from them in melting point and in its ready esterifiability.

The acid, its esters and other derivatives, when pure, are odorless, but ordinarily have a faint pleasant smell. A drop of the acid, with acetic acid, concd. sulfuric acid and chloroform, gives a light red coloration similar to chaulmoogric acid, while rosin in this test gives a deep violet.

When exposed to the air, especially in thin layers, cativic acid shows surface hardening, and the films are transparent, fairly soft, elastic solids, having largely lost their tackiness. This hardening (also with glyceryl cativate) occurs even in stoppered bottles. Cativic acid does not darken in the air at room temperature even after several years, but does so rapidly at higher temperatures.

Salts of Cativic Acid

The acid is monobasic and forms salts readily by the regular methods. The alkali salts are soluble in water, alcohol and their mixtures, but insoluble in acetone, ether, and paraffin hydrocarbons. They are stable even on heating to 270° (1.5 mm.), are hydrolyzed in aqueous solution, have a good detergent action, but evolve the sticky acid. Electrolytes precipitate the alkali salts as jellies. The other metallic salts are colorless, or have their cation color, and are thermoplastic powders. They may be prepared by metathesis or sometimes by dissolution of the metal oxide in the hot acid. They are insoluble in water and also (or slightly soluble) in acetone, methyl and ethyl alcohols. They are readily soluble in the aromatic and higher aliphatic hydrocarbons. The zinc, manganous, lead, cupric and ferric salts are soluble in the ester type solvents such as ethyl acetate. They are very soluble in the chlorinated hydrocarbon solvents and in turpentine. They dissolve in vegetable oils (linseed, tung) on heating and do not separate on cooling, although apparently insoluble when cold.

Ammonium Cativate.—This salt is useful for purification purposes. A petroleum ether solution of cativo is filtered, dried and the salt precipitated by passing in anhydrous ammonia. The supernatant solution is decanted, the precipitate decomposed with acid and the process repeated with the free acid for further purification. If the jelly-like ammonium cativate–petroleum ether solution is centrifuged, it becomes homogeneous, showing no separation even in a year's time. Evaporation of an aqueous solution to dryness yields the free acid by hydrolysis.

Polyvalent and Heavy Metal Salts.—These may be prepared from the alkali salts by metathesis, or directly from impure or purified cativo. Solution of cativo in alcohol, filtration, neutralization (with or without saponification) with aqueous or alcoholic alkali and addition of an aqueous or alcoholic solution of the heavy metal salt precipitates the cativate along with cativyl cativate or cativyl alcohol (and the ethereal oil present), which latter are extractable with acetone, leaving the salt with the 0.5% impurity of low-boiling acid salt. A pure salt results if the cativo is first freed from impurities by heating to 100° in a 5-mm. vacuum. These salts also may be prepared by heating cativo, cativic acid or its esters to 100–200°, with or without a high-boiling solvent such as "Varnolene," and adding the metallic oxide or hydroxide. The water produced boils off rapidly. The presence of an inert atmosphere is desirable, as also is the solvent, since without a solvent a rather unwieldy mass results before the reaction is complete.

Esters of Cativic Acid.—In contrast to the resin acids, cativic acid is esterified easily in excellent yields.

The lower alkyl esters, butyl for example, may be prepared by dissolving cativo in butyl alcohol, adding 2% of concd. sulfuric acid and heating on the steam-bath for three hours. The sulfuric acid is neutralized and the mixture subjected to fractional vacuum distillation, the excess alcohol and impurities coming off first, giving a 98% yield of butyl cativate with an acid number of 2.2 (showing 1.2% of unesterified cativic acid).

The esters of monomethyl-, monoethyl- and monobutylethylene glycol ethers may be prepared from the acid, using anhydrous hydrogen chloride as catalyst. With higher boiling alcohols (glycerol, diethylene glycol), cativic acid may be heated directly with the alcohol, in a partial vacuum of nitrogen or carbon dioxide, and with aluminum foil. The reaction with glycerol, for example, goes well at 210–230° (150–250 mm.) with two hours of refluxing of the glycerol. The water produced boils off rapidly, cessation indicating completion of the reaction, and any excess of glycerol may be distilled off in 1–10 mm. vacuum.

The pure esters are water-white and odorless; less pure samples, particularly of the heavier molecules, are yellow in color and have a faint sweetish odor. The methyl to isoamyl and cellosolve esters are limpid liquids, the ethylene and triethylene glycol esters more viscous, the mono- and diacetine esters still more so, and the glyceryl ester is almost solid when cold (thermoplastic).

PROPERTIES AND ANALYSES OF ESTERS

Cativates	Viscosity[b] 23.5°	Ref. index	Approx. b. p., °C.	Mm.	Sp. gr. 21°	Ester no. Calcd.	Found	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
Methyl	170.6	1.4967	200	1	0.985	175.3	175.2	78.68	78.85	11.33	11.26
Ethyl		1.4910	206	2.5	.980						
n-Butyl[a]	129.6	1.4890	208	2.75	.965	154.9	155.6	79.48	79.16	11.69	11.75
Isoamyl			221	3.5	.953						
Methylcellosolve	167.6	1.4897	243	23	.982	154.0	152.1				
Cellosolve	143.4	1.4854	212	1.75	.980	148.3	149.5				
Butylcellosolve			240	2.5	.967						
Triethylene glycol di-			312	1.5	1.015						
Glyceryl tri-					1.000						

[a] Mol. wt. calcd., 362; found (b. p. method), 354. [b] Water value, 17.8 scc.

The esters are insoluble in water and generally soluble in and miscible with butanol, methyl, ethyl and butyl acetates, ethyl and petroleum ethers, aliphatic and aromatic hydrocarbons, acetone and methyl ethyl ketone and in various chlorinated solvents. Some are soluble in methanol and ethanol, but methyl cativate is sparingly soluble in methanol, isoamyl cativate insoluble and triethylene glycol dicativate nearly insoluble in ethanol, and glyceryl tricativate insoluble in methanol and nearly so in ethanol.

Methyl, *n*-butyl, cellosolve, methylcellosolve, glyceryl and mixed glyceryl with cativyl, cativates were boiled with water for eight hours. Since acid numbers taken before and after this treatment were unchanged, it seems that the esters undergo no real hydrolytic cleavage.

The cativate esters are compatible with many commercial products: they may be added to nitrocellulose or ethylcellulose, even up to two parts of ester of one of cellulose derivative, improving the quality of the product. The esters also may be used as plasticizers for water insoluble metal cativates and other products.

Dihydroxycativic Acid.—Cativic acid is dissolved in a slight excess of concd. sodium hydroxide solution, water added and enough cracked ice to give a 2% sodium salt concentration. The calculated amount of a 5% potassium permanganate solution is added slowly with stirring, keeping the temperature at 0–5°. The manganese dioxide sludge is filtered off, the solution acidified with sulfuric acid and the liquid decanted from the precipitated acid, which is dried and caused to crystallize by trituration with petroleum ether. The product is dissolved in benzene and filtered hot, giving on cooling colorless, fluffy needles, m. p. 158°.

Anal. Calcd. for $C_{20}H_{36}O_4$: C, 70.53; H, 10.67; mol. wt., 340; acid no., 164.9. Found: C, 70.29; H, 10.50; mol. wt. (f. p. in camphor), 336; acid no., 165.2.

Methyl Ester.—The acid is difficultly soluble in methyl alcohol, but if the resulting dilute solution is treated with hydrogen chloride esterification follows. The addition of water precipitates a neutral white powder, which forms beautiful long needles when its methyl alcohol solution is allowed to evaporate slowly, m. p. 64°; ester no., calcd. 158.4, found 158.2.

If methyl dihydroxycativate is heated, it loses a molecule of water and vacuum distillation then gives an oily neutral ester.

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.95; H, 10.79. Found: C, 74.79; H, 10.86.

Summary

1. Cativo resin has been shown to consist almost entirely of cativic acid, $C_{20}H_{34}O_2$, and the corresponding ester, cativyl cativate.

2. Metal salts and various esters of cativic acid have been prepared and described, as well as dihydroxycativic acid.

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