TABLE 11[a]

β-METHYL-β-MONOALKYLAMINOPROPYL CINNAMATE, HYDROCINNAMATE, ALKOXYCINNAMATE AND ALKOXYHYDROCINNAMATE HYDROCHLORIDES, $ArCOOCH_2C(CH_3)_2NHR \cdot HCl$

Acid (Ar)	R	M. p., °C. (cor.)	Molecular formula	Chlorine, % Calcd.	Chlorine, % Found[b]	Free base B. p., °C.	Free base Mm.	Free base Nitrogen, % Calcd.	Free base Nitrogen, % Found[c]
Cinnamic	*n*-Propyl	164–165	$C_{16}H_{24}O_2NCl$	11.91	12.07				
Cinnamic	*n*-Butyl	162–163	$C_{17}H_{26}O_2NCl$	11.37	11.19				
Cinnamic	*n*-Amyl	112–113	$C_{18}H_{28}O_2NCl$	10.88	11.20				
Hydrocinnamic	*n*-Propyl	178–179	$C_{16}H_{26}O_2NCl$	11.82	12.12	177–178	3.5	5.32	5.50
Hydrocinnamic	*n*-Butyl	116–117	$C_{17}H_{28}O_2NCl$	11.29	11.59				
Hydrocinnamic	*n*-Amyl	85–86	$C_{18}H_{30}O_2NCl$	10.81	10.60	181–188	2.8	4.80	4.42
Hydrocinnamic	*n*-Hexyl	90–91	$C_{19}H_{32}O_2NCl$	10.37	10.05				
p-Methoxycinnamic	Ethyl	189–190	$C_{16}H_{24}O_3NCl$	11.30	11.38				
p-*n*-Butoxycinnamic	*n*-Propyl	144–145	$C_{20}H_{32}O_3NCl$	9.59	10.14				
	n-Butyl	154–155	$C_{21}H_{34}O_3NCl$	9.24	9.18				
o-Ethoxyhydrocinnamic	*n*-Propyl	Oil				193–196	3.0	4.56	4.32
p-*n*-Propoxyhydrocinnamic	*n*-Butyl	95–96	$C_{20}H_{34}O_3NCl$	9.53	9.83				
p-*n*-Butoxyhydrocinnamic	*n*-Butyl	109–111	$C_{21}H_{36}O_3NCl$	9.19	9.57				

[a] In this table are listed only the amino alcohol esters which were satisfactorily purified by recrystallization of the hydrochloride or distillation of the free base. These products are being tested pharmacologically by Dr. H. B. Haag, of the Medical College of Virginia, and will be reported elsewhere. [b] Chloride was determined by the Volhard method as modified by J. R. Caldwell and H. V. Moyer, *Ind. Eng. Chem., Anal. Ed.*, 7, 38, 39 (1935). [c] Nitrogen was determined by titration of the free base with standard hydrochloric acid, with modified methyl red as indicator.

quantities (0.15 mole) of *o*-ethoxyhydrocinnamic acid and phosphorus pentachloride on a boiling water-bath for one hour. The phosphorus oxychloride was removed by vacuum distillation and the acid chloride was purified by vacuum distillation.

Hydrochlorides of β-Methyl-β-monoalkylaminopropyl Cinnamates, Alkoxycinnamates, Hydrocinnamates and Alkoxyhydrocinnamates.—The β-monoalkylamino-β-methylpropanols were prepared and condensed with aroyl halides by methods described in previous publications[2,3] from this Laboratory. Equimolar quantities of amino alcohol hydrochlorides and aroyl halides were heated on a water-bath from one to six hours, depending on the rate of reaction. In a few cases an oil-bath, heated gradually to 150°, was used. As in previous reports, the reaction mixture was dissolved in water, filtered and extracted with isopropyl ether to remove impurities, and treated with sodium hydroxide to set free the amino alcohol esters. These esters were taken up in isopropyl ether and the hydrochlorides precipitated by addition of dry hydrogen chloride. Various solvents were used for recrystallization but a mixture of anhydrous acetone and anhydrous ether proved satisfactory in most cases. In a few cases in which recrystallization of the hydrochloride of the amino alcohol ester did not take place readily, the free base was purified by vacuum distillation.

Summary

The hydrochlorides of a series of β-methyl-β-monoalkylaminopropyl cinnamates, hydrocinnamates, alkoxycinnamates and alkoxyhydrocinnamates have been prepared and described.

RICHMOND, VA. RECEIVED AUGUST 25, 1947

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

The Occurrence of Rutin in a Wild Cherry, *Prunus melanocarpa* (A. Nels.) Rydb.

BY JAMES F. COUCH

In connection with the researches being conducted at this Laboratory[2] on the production of rutin for medicinal use a species of wild cherry was examined with the result that significant quantities of rutin were found in the leaves. This is the first species of the genus *Prunus* from which this glucoside has been isolated, although the presence of other flavonol glucosides in different species of the genus has been reported.

Rochleder[3] found a trace of a quercetin glucoside in *P. cerasus* L., and Finnemore[4] isolated quercimeritrin from a commercial bark probably of *P. emarginata* Walp. Power and Moore[5] obtained less than 0.1% of a quercetin glucoside which they named serotrin from the leaves of *P. serotina* Ehrh. This substance melted at the same temperature as quercimeritrin but on comparison with an authentic sample the authors concluded that it was a different substance.

Rutin has now been found in the leaves of "black chokecherry" (*P. melanocarpa* (A. Nels.) Rydb.) in substantial quantities. This species ranges from Alberta and British Columbia southward to California and New Mexico[6] in accessible

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(1) One of the Laboratories of the Bureau of Agricultural & Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture. Article not copyrighted.

(2) J. F. Couch, C. F. Krewson, J. Naghski and M. J. Copley, *Bur. Agri. Ind. Chem.*, AIC-115, April, 1946. [Processed.]

(3) F. Rochleder, *S-Ber. Wien. Acad.*, Abt. II, **59**, 219–247 (1869).

(4) H. Finnemore, *Pharm. J.*, **85**, 604–607 (1910).

(5) F. B. Power and C. W. Moore, *J. Chem. Soc.*, **97**, 1099–1112 (1910).

(6) I. Tidestrom, *Flora of Utah and Nevada*, "U. S. Natl. Herbarium," Vol. 25, Gov't. Printing Office, Washington, D. C., 1925, p. 285.

localities and may prove to be a commercial source of the drug. Several samples of leaves collected at different stages of growth and at two different altitudes were examined. The leaves were collected in 1936 and 1937 near the Salina Experiment Station, Salina, Utah, in connection with studies on poisoning of livestock by cyanogenetic plants. They were air dried and had been stored in the laboratory for ten years. Crude rutin was obtained from a composite lot of these samples in 1937 but was not investigated further at that time. Analyses of the samples are in Table I.

TABLE I

Lot no.	Date collected, 1936	Approximate altitude, ft.	Moisture,[7] %	Rutin,[7] % mfb
47-7	June 15	8000	6.00	1.57
47-6	Aug. 17	8000	7.20	1.44
47-9	Aug. 20	8500	6.15	3.13
47-10	Composite	8000	7.60	1.63
	1937			
47-8	June 17	8500	6.40	3.88

The figures indicate a considerably greater content of rutin in leaves collected at the higher altitude but do not show much difference between young (June collections) and older (August) leaves.

Experimental

A quantity of the air-dried leaves (6,646 g.) was coarsely powdered, moistened with alcohol and extracted in a glass percolator with alcohol. The solvent was distilled from the percolate and the greenish residue was thoroughly extracted with boiling distilled water. The water solution was filtered from the fatty materials and allowed to cool. After standing several days a considerable quantity of brown flocculent material separated. This was filtered and redissolved in boiling water. The filtered solution deposited the substance on cooling. The crude rutin (24.0 g.) was greenish in color and contained 88% of the pure glucoside. This was bottled and preserved for several years. The rutin (2 g.) was purified by dissolving in alcohol (50 ml.), filtering from some amorphous matter, and diluting to 500 ml. with water containing 2 ml. of concentrated hydrochloric acid. The rutin which slowly precipitated during the ensuing twenty-four hours was of bright yellow color and crystallized in the characteristic microscopic fan-shaped bundles of needles. It was filtered, washed with water and dried at 110°. The plastic range ("melting point") was 172-174° raised by recrystallization from alcohol and from water to 190-192°. A spectrophotometric examination by W. L. Porter identified the substance as rutin by the following constants: The ultraviolet absorption spectrum of the anhydrous sample was characterized by absorption maxima near 3627 and 2577 Å., specific extinction coefficient, 32.6 liter g.$^{-1}$ cm.$^{-1}$ at 3627 Å., extinction ratio of 0.875 for wave lengths 3752 and 3627 Å. The corresponding figures for authentic rutin are: 3627 and 2577 Å., 32.5 at 3627 Å. and 0.875.

Anal.[8] Calcd. for $C_{27}H_{30}O_{16}$: C, 53.11; H, 4.95. Found: C, 52.92; H, 4.99.

Summary

Rutin has been isolated in significant quantities from black chokecherry, a species native to the mountain region of the western United States.

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[7] Analyses made by C. S. Fenske, Jr., of this Laboratory.

[8] Analysis by C. L. Ogg.

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[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

Isolation of Rutin from a Citrus Hybrid

BY C. F. KREWSON AND J. F. COUCH

The discovery of Szent-Györgyi and co-workers[2] that citrus fruits contain a substance not identical with hesperidin or any other identified constituent of these fruits has led to much chemical and physiological research in an endeavor to isolate and characterize the active compound, which has been termed vitamin P.[3] Investigations begun in 1943 have established the fact that rutin, a flavonol glucoside present in some forty species of plants, has the physiological activity attributed to vitamin P.[4] The question whether the activity reported from citrus fruits which may be due to the presence of rutin has been investigated in this Laboratory. Valencia oranges, grapefruit and both green and ripe lemons, reported to be most active of the citrus fruits with respect to vitamin P activity, have been examined without revealing the presence of rutin. These have been subjected to three extraction procedures: the usual alcoholic technique,[5] a special process involving enzymatic hydrolysis of pectin, and an alkali extraction. In no case was rutin found by the alcoholic extraction. In the instance of a hybrid fruit, rutin was found by the other two processes, the alkali extraction described below being more effective.

Two years ago we obtained from the orchard of A. C. Krewson, Plymouth, Florida, specimens of a citrus fruit of the size and form of grapefruit but with a distinct odor and flavor of the lemon. The

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[2] P. L. Armentano, *et al.*, *Deut. Med. Woch.*, **62**, 1326-1328 (1936).

[3] V. Bruckner and A. Szent-Györgyi, *Nature*, **138**, 1057 (1936).

[4] J. Q. Griffith, Jr., J. F. Couch and M. A. Lindauer, *Proc. Soc. Exptl. Biol. Med.*, **55**, 228-229 (1944); J. F. Couch, C. F. Krewson, J. Naghski and M. J. Copley, U. S. Department of Agriculture, Mimeograph Circular AIC-115, April, 1946.

[5] J. F. Couch and C. F. Krewson, U. S. Department of Agriculture Mimeograph Circular AIC-52, July, 1944.