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

# Isolation of Rutin from Two Varieties of *Forsythia*

BY J. NAGHSKI, W. L. PORTER AND J. F. COUCH

Eykman[2] in 1886, during the course of an examination of *Forsythia suspensa* Vahl,[3] obtained a yellow powder which he concluded was quercetin "by its reactions" but which was undoubtedly rutin. At that time these two substances were frequently mistaken for each other.

Rutin ($C_{27}H_{30}O_{16}\cdot 3H_2O$) was first reported from the genus *Forsythia* in 1929 by Gollan,[4] who isolated it in 0.35–0.37% yield from the fresh flowers of *F. pendula* L. This work appears to have been overlooked. In 1936 Czimmer[5] isolated from the flowers of *F. suspensa viridissima* a flavonol glucoside which she did not identify but which was undoubtedly rutin, since, although the melting point was low, its other physical and chemical properties and crystal habit agreed with those of rutin. Recently Schindler[6] reported the isolation of a "diglucoside of quercetin" from dried flowers of *F. suspensa* Vahl. He gives no evidence of a search for rhamnose among the hydrolytic products of his glucoside, reporting only dextrosazone, and concluding that the substance yields 2 moles of dextrose on hydrolysis. The optical rotation was high, and the melting point was low; otherwise the properties of the substance as reported were those of rutin.

In connection with the work on rutin at this Laboratory[7] and the clinical studies on the medical applications of this glucoside,[8,9] the rutin contents of two varieties, *Forsythia suspensa* Vahl and *F. fortunei* Rehd, were determined in 1945. Collections were made in the neighborhood of Philadelphia. Rutin was isolated from the young fresh blossoms of both varieties, *suspensa* yielding 1.09% and *fortunei* 4.29%. Specimens of *fortunei* collected eight days after the first collection, when the blossoms were more mature, contained only traces of the glucoside (Table I). It was identified as rutin by its chemical and physical properties and by comparison with authentic specimens derived from buckwheat, tobacco and elder.

These observations were checked in 1946 on blossoms of *F. fortunei*. Rutin in a yield of 2.08% was obtained from this sample.

TABLE I

RUTIN IN *Forsythia* BLOSSOMS

| Date | Variety | Moisture, % | Rutin, % (m. f. b.) |
|---|---|---|---|
| 3/22/45 | *F. suspensa* | 85.4 | 1.09 |
| 3/23/45 | *F. fortunei* | 85.4 | 4.29 |
| 3/31/45 | *F. fortunei* | 87.1 | Trace |
| 3/27/46 | *F. fortunei* | 86.0 | 2.08 |

## Experimental

Eight hundred forty grams of fresh blossoms (117.5 g. dry weight) were extracted with ethanol in Soxhlet extractors. The alcohol extracts were concentrated under reduced pressure to about 300 ml.; 200 ml. of distilled water was added, and the solution was again concentrated to 300 ml. to remove the last traces of alcohol. The solution was quickly filtered through paper. Since microscopic examination showed that the filtrate contained a considerable quantity of emulsified fatty materials, it was extracted twice with 75-ml. portions of ether in a separatory funnel. Upon standing at room temperature for two days, the aqueous solution deposited 2.33 g. (dry) of yellow needles, characteristic of rutin. A further crop, 0.12 g., was obtained by re-extracting the water-insoluble materials with boiling water. The yield was 2.45 g., or 2.08% of the moisture-free blossoms.

The dried crystals were dissolved in 15 ml. of absolute ethanol, and the small quantity of insoluble material was filtered off. The alcohol filtrate was diluted to 200 ml. with distilled water. When the solution became cloudy from crystallization, it was filtered with suction. Previous experience has shown that finely divided impurities which escape previous filtration are removed by adsorption on the first few crystals of rutin. The filtrate crystallized overnight, and the crop of crystals obtained weighed 1.94 g. (dry). These crystals were then recrystallized once from boiling water. The plastic range ("melting point") was 189–191.5° corrected.

**Spectrophotometric Identification of the Glucoside.**—Spectrophotometric examination of this material showed it to be rutin slightly contaminated with quercetin and an unidentified sterol-like material. Extraction with Skellysolve B and then with ethyl ether and recrystallization again from water did not completely remove the impurities. Spectrophotometric examination of the extracted material gave the following constants: $k_{362.7}$,[10] 32.38; $k_{362.7}/k_{375.2}$, 0.888; which indicate the following composition: rutin, 95.6%; quercetin, 2.8%; and unknown, 1.6%. Pure rutin gives $k_{362.7}$, 31.90; $k_{362.7}/k_{375.2}$, 0.875 ± 0.004.[11]

**Chemical Identification of the Glucoside.**—The glucoside (0.324 g.) was hydrolyzed with sulfuric acid, and the hydrolytic products were characterized. The aglycone melted at 314–315° and gave an acetyl derivative; m. p., 195–196.5°. A mixture with quercetin pentaacetate (m. p., 195–196.5°) melted at 195–196.5°.

Phenylosazones of the sugars were prepared and fractionated with acetone.[12] The acetone-soluble fraction after recrystallization from hot 5% pyridine and hot 20% ethanol melted at 180–183°. The mixed melting point with rhamnosazone (m. p., 179–180°) was 179–180°. The acetone-insoluble fraction, also recrystallized from

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[1] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture.

[2] Eykman, *Rec. trav. chim.*, **5** 127–139 (1886).

[3] The botanical names are those used by the authors quoted and may be inaccurate.

[4] Gollan, *Bull. soc. chim. biol.*, **11**, 1164–1169 (1929).

[5] Czimmer, *Arch. Exp. Path. Pharm.*, **183**, 587–594 (1936).

[6] Schindler, *Helv. Chim. Acta*, **28**, 1157–1159 (1945).

[7] J. F. Couch and C. F. Krewson, Rutin, U. S. D. A. Bureau of Agricultural and Industrial Chemistry, AIC-52, July 1944; J. F. Couch, J. Naghski and C. F. Krewson, *Science*, **103**, 197–198 (1946).

[8] J. Q. Griffith, Jr., J. F. Couch and M. A. Lindauer, *Proc. Soc. Exp. Biol. Med.*, **55**, 228–229 (1944).

[9] R. L. Shanno, *Am. J. Med. Sci.*, **211**, 539–543 (1946).

[10] The symbol $k_{362.7}$ is the optical density at 362.7 mμ referred to unit thickness (cm.) and unit concentration (g./liter).

[11] W. L. Porter, B. A. Brice, J. F. Couch and M. J. Copley, "The Spectrophotometric Determination of Rutin in Various Preparations," in press.

[12] A. G. Perkin, *J. Chem. Soc.*, **97**, 1776–1778 (1910).

5% pyridine and 20% ethanol, melted at 202°. The mixed melting point with glucosazone (m. p., 207–208°) was 204–204.5°.

## Summary

Rutin was isolated from the fresh flowers of two varieties of *Forsythia*, *suspensa* and *fortunei*, and identified by chemical and spectrophotometric methods. Evidence was obtained that the rutin content diminishes with age in *F. fortunei* as it does in buckwheat.

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[CONTRIBUTION FROM THE CENTRAL RESEARCH LABORATORIES, MONSANTO CHEMICAL COMPANY]

# Unsaturated Nitriles. IV. Adducts of Dienes with Fumaronitrile[1]

BY DAVID T. MOWRY

It has been well established that the cyano group confers considerable dienophilic activation upon a double bond in the $\alpha,\beta$-position.[2] Acrylonitrile,[3] crotononitrile[4] and alkylidene malonitriles[5] have been shown to condense with dienes. Recently Blomquist and Winslow[6] have condensed cyclopentadiene and diphenylfulvene with dinitriles such as fumaronitrile, maleonitrile and acetylene dicarbonitrile.

The present paper reports an extension of the work with fumaronitrile in which a variety of dienes were used. Fumaronitrile has been found to form adducts with cyclopentadiene, 2-methylpentadiene, allo-ocimene, anthracene, furan, sylvane, 2,5-dimethylfuran, furfuryl acetate and ergosterol. In addition isosafrole and methyl abietate gave indications of having formed adducts but no well-defined crystalline or distillable products could be isolated from the reaction mixture.

3,6-Methano-1,2,3,6-tetrahydrophthalonitrile (from cyclopentadiene and fumaronitrile) was further characterized by the preparation of a dichloride.

TABLE I

| | | | | Analyses, %[a] | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Carbon | | Hydrogen | | Nitrogen | |
| 1,2,3,6-Tetrahydrophthalonitrile | Yield,[e] % | M. p., °C. | Formula | Calcd. | Found | Calcd. | Found | Calcd. | Found |
| 3,6-Methano- | 98 | 98[b] | $C_9H_8N_2$ | .. | .. | .. | ... | ... | ... |
| 3,5-Dimethyl- | 40 | 68[f] | $C_{10}H_{12}N_2$ | 75.0 | 74.8 | 7.50 | 7.43 | 17.50 | 17.66 |
| 3,3-Dimethyl-6-($\alpha$-methylpropenyl)[c] | 23 | 98 | $C_{14}H_{18}N_2$ | 78.5 | 78.4 | 8.42 | 8.52 | 13.07 | 13.08 |
| 3,6-Endoxo- | 25 | 111 | $C_8H_6ON_2$ | 65.7 | 66.0 | 4.13 | 4.52 | 19.30 | 19.11 |
| 3-Methyl-3,6-endoxo- | 20 | 100 | $C_9H_8ON_2$ | 66.7 | 67.0 | 4.97 | 5.38 | 17.28 | 17.68 |
| 3,6-Dimethyl-3,6-endoxo- | 24 | 72 | $C_{10}H_{10}ON_2$ | 69.0 | 69.0 | 5.75 | 6.04 | 16.08 | 16.19 |
| 3-Acetoxymethyl-3,6-endoxo- | 23 | 113 | $C_{11}H_{10}O_3N_2$ | 60.6 | 60.5 | 4.63 | 4.76 | 12.83 | 12.93 |
| 3,6-Methano-1-methyl- | 44 | 127[g] | $C_{10}H_{10}N_2$ | 76.0 | 75.8 | 6.38 | 6.67 | 17.74 | 18.06 |
| Other adducts | | | | | | | | | |
| 9,10-($\alpha,\beta$-Dicyanoethano)-9,10-dihydroanthracene | 64 | 259 | $C_{18}H_{12}N_2$ | 84.4 | 84.3 | 4.72 | 4.87 | 10.94 | 10.96 |
| 5,8-($\alpha,\beta$-Dicyanoethano)-5,8-dihydroergosterol | 40 | 210–212 | $C_{32}H_{46}ON_2$ | 81.0 | 80.7 | 9.75 | 10.10 | 5.91 | 5.71 |
| 3,6-Methano-4,5-dichlorohexahydrophthalonitrile | 78 | 167 | $C_9H_8N_2Cl_2$ | .. | [d] | .. | ... | 12.96 | 12.95 |

[a] Microanalyses by the Arlington Laboratories, Fairfax, Va. [b] Blomquist and Winslow, ref. 6, give m. p. 96°. [c] This structure is preferred to the alternative 3,4-dimethyl-6-isobutenyl-1,2,3,6-tetrahydrophthalonitrile because the analogous anhydride is obtained from allo-ocimene and maleic anhydride, see Alder, *Die Chemie*, **55**, 53 (1942), and Hultzsch, *Ber.*, **72B**, 1173–1187 (1939). [d] Calcd. for Cl, 32.8; found, 33.1. [e] No allowance made for unreacted reagents which were recovered. [f] B. p. 138° (3 mm.). [g] B. p. 158–160° (20 mm.).

Cyclopentadiene was also condensed with mesacononitrile, which proved to be less reactive than fumaronitrile, to give 3,6-methano-1-methyl-1,2,3,6-tetrahydrophthalonitrile.

The compounds prepared are listed and described in Table I. The adducts of fumaronitrile with the lower diolefins were reasonably stable and could be distilled under reduced pressure. On the other hand, the compounds obtained from the furan derivatives decomposed at temperatures somewhat above their melting points. Thus, when 1,2,3,6-tetrahydro-3,6-endoxophthalonitrile was heated a short time at 115° a nearly quantitative dissociation into furan and fumaronitrile

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(1) Preceding papers, THIS JOURNAL, **66**, 371 (1944); **67**, 926, 1050 (1945).

(2) See Norton, *Chem. Rev.*, **31**, 319 (1942); Alder, *Die Chemie*, **55**, 53 (1942).

(3) Wolfe, U. S. Patent 2,217,632 (1940); Miller and Bradley, U. S. Patent 2,382,803 (1945).

(4) I. G. Farbenindustrie A.-G., French Patent 37,498 (1929).

(5) Alder and Rickert, *Ber.*, **72B**, 1983 (1939), U. S. Patent 2,264,354 (1941).

(6) Blomquist and Winslow, *J. Org. Chem.*, **10**, 149 (1945).