Alkaloids of the Bark of *Teclea grandifolia*

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The bark of *Teclea grandifolia* Engl. was found to contain evoxanthine, norevoxanthine, and an unidentified alkaloid.

In 1957, GELLERT (1) reported on the constituents of the bark of *Teclea grandifolia* Engl. *Rutaceae*. In addition to identifying a number of nonalkaloidal constituents, Gellert reported the presence of about 1.2% alkaloids in the stem bark of *T. grandifolia*. However, this material was stated to be amorphous in character and was not further examined. In 1958, Paris and Stambouli (2) reported that the roots of *T. grandifolia* contained the alkaloid evoxanthine. In view of the medicinal use of *T. grandifolia* in Africa (1) and the presence of alkaloids in related genera, we now report an extension of Gellert's investigation of the stem bark of *T. grandifolia*.

The ground stem bark was extracted with naphtha to remove the nonalkaloidal constituents, and the residue was extracted continuously with 90% ethanol. The residue remaining after concentration of the ethanol extract was digested with acid and the acidic solution brought to pH 8. At this pH a precipitate was collected and chromatographed to give an alkaloid, m.p. 217–218°, in 0.04% yield. This material was homogeneous by paper chromatography (3). Its ultraviolet and infrared spectra were identical with evoxanthine; it did not depress the melting point of an authentic sample of evoxanthine.

The residual remaining after the acid digestion was extracted with methylene chloride to give after chromatography an alkaloid, m.p. 274–275°, in 0.006% yield. This alkaloid gave derivatives, tests, and spectra consistent with that of norevoxanthine (4). That it was norevoxanthine was confirmed by its conversion to evoxanthine on treatment with diazomethane.

After precipitation of the crude evoxanthine at pH 8, a chloroform extraction of the basic solution yielded after chromatography a trace of yellow solid, m.p. 185°, in less than 0.002% yield. This nitrogen containing material was homogeneous on paper chromatography, gave a positive Lebat test, had ultraviolet maxima at 208 and 278 mμ (95% ethanol) and the infrared spectra included bands at 3600 and 1620 cm.$^{-1}$ Sufficient material for further identification was not available.

While a total ethanol extract of the bark and a total naphtha extract of the bark both exhibited some activity against cell culture (KB line) (ED_{50} of 3.0×10^1 and 6.2×10^0 mcg./ml., respectively), evoxanthine itself was inactive (ED_{50} of $>1.0 \times 10^2$ mcg./ml.).[1] The total ethanol extract exhibited no activity or toxicity against the Dunning leukemia in Fisher rats.[2]

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EXPERIMENTAL

Plant Material.—The tree bark (trunk) of *T. grandifolia* was supplied by the Silviculturist, Ghana. A small amount of the initial material was supplied by Dr. Gellert (1).

Extraction and Isolation.—The dried powdered bark was extracted first with naphtha and then with 90% ethanol. The ethanol extract was concentrated *in vacuo* and the concentrate digested with 8% hydrochloric acid. The acidic digest was filtered, brought to pH 8 with sodium carbonate, and a dirty green precipitate obtained. Chromatography of this precipitate over alumina (Merck, reagent chromatographic aluminum oxide) gave, with chloroform as the eluent, a solid (0.04% yield), m.p. 217–218° (from ethyl acetate). The R_f on paper chromatography using butanol:acetic acid:water (4:1:1) was 0.87 (3). This material was identical in every respect with an authentic sample of evoxanthine. The powdered residue obtained after the hydrochloric acid digestion of the ethanol extract was extracted with methylene chloride. Concentration of the methylene chloride gave a solid (0.006%), m.p. 274–275° [reported (4) for norevoxanthine, m.p. 275°]. This material appeared to be identical tc norevoxanthine in all of its reactions. That it was norevoxanthine was confirmed by reacting it with diazomethane in methanol to give evoxanthine. The norevoxanthine had an R_f of 0.79 in the above solvent system. The basic solution left after the precipitation of the crude base at pH 8 was extracted with chloroform, and the concentrated extract was chromatographed over alumina (Merck) to give in the methanol eluate a material (0.002%), m.p. 185°, with an R_f of 0.72 in the above solvent system. This material contained nitrogen and gave a positive Lebat test. The details of its spectra are included in the text.

A number of other extraction schemes were tried with the same qualitative results. Solid nitrogen containing compounds with R_f for other than 0.87, 0.79, and 0.72 were not obtained. Traces of noncrystalline materials with R_f of 0.58 and 0.69 were observed in some cases.

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[1] Results supplied by the C.C.N.S.C., National Institutes of Health.
[2] Results supplied by Dr. Leo Rane, University of Miami.