

ISOLATION OF (-)-HARDWICKIIC ACID AND 1-TRIACONTANOL FROM *CROTON CALIFORNICUS*

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Croton californicus Muell. Arg. (Euphorbiaceae) is an herbaceous shrub indigenous to the Sonoran Desert. Indians prepare a hot poultice from the powdered leaves as a pain reliever for rheumatism (1). An extensive literature search revealed that *C. californicus* has been screened for alkaloids, flavonoids, and saponins-negative, and tannins-positive (2). It was found that the chloroform extract demonstrated antimalarial activity (3).

As a result of a phytochemical investigation of *C. californicus*, it was found that the ethanol extract of the dried whole plants contained the furanoid diterpene, (-)-hardwickiic acid, and the long chain alcohol, 1-triacontanol. (-)-Methylbarbascoate, previously isolated and characterized from *C. californicus* by Wilson *et al.* (1) and hardwickiic acid are closely related diterpenes of the trans clerodane class. While (-)-hardwickiic acid has been found to be present in *Croton oblongifolius* (4), this is the first reported occurrence of both (-)-hardwickiic acid and 1-triacontanol in *Croton californicus*.

EXPERIMENTAL²

PLANT MATERIAL.—Roots, stems, leaves,

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²Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. The infrared spectra were obtained on a Beckman IR-33. The pmr spectra were determined on a Varian EM-360L using tetramethyl silane as an internal standard. Mass spectra were obtained on a Finnegan 300-6110 Quadrapole gas chromatograph-mass spectrometer. The optical rotation was taken on a Perkin-Elmer 241 MC Polarimeter. Carbon, hydrogen analyses were performed by Chemalytics, Inc., 2330 S. Industrial Park Dr., Tempe, Arizona.

flowers, and fruits of *Croton californicus* Muell. Arg. were collected near Yuma, Arizona, during September, 1975. Identification was confirmed by Dr. Robert E. Perdue, Chief, Medicinal Plant Resources Laboratory, U.S.A., Beltsville, MD. A reference specimen is maintained by the Herbarium of the National Aboetum, Agricultural Research Station, U.S. Department of Agriculture, Washington, D.C.

EXTRACTION AND FRACTIONATION.—Dried whole plants of *C. californicus* (14 kg) were ground and extracted exhaustively with 95% ethanol in a Lloyd-type extractor to yield 1.3 kg of air dried extract. The ethanol extract was subsequently partitioned between petroleum ether and 20% aqueous methanol (1:1). A portion (50 gm) of the petroleum ether fraction was chromatographed over a 7 x 65 cm column of silica gel 60 (Merck; 1.3 kg) eluted with a hexane ether gradient (20→50% ether).

ISOLATION OF (-)-HARDWICKIIC ACID.—Fractions 5 to 52 (250 ml each) of the 20% ether-hexane eluent were combined, evaporated *in vacuo*, and the resulting residue (3.8 g) chromatographed over a silica gel 60 column (4 x 38 cm; 190 gm) with hexane-ether-acetic acid (40:5:0.5) as the eluent. From fractions 1 to 10 (25 ml each) a residue was obtained which crystallized readily from hexane as colorless crystals (265 mg), mp 99–100° [lit. 106–107° (6)], $[\alpha]_D^{25} - 116.5^{\circ}$ (conc. 1.09, EtOH); ir ν max (CHCl₃) 3300–2500, 1680, 1632, 1015, 868 cm⁻¹; pmr (CDCl₃, 60 MHz) δ 10.75 (s, 1H), 7.27 (t, 1H, $J = 1.5$ Hz), 7.17 (s, 1H), 6.8 (t, 1H, $J = 4$ Hz), 6.2 (s, 1H), 1.26 (s, 3H), 0.87 (d, 3H, $J = 6$ Hz), 0.76 (s, 3H); ms m/e 316 (M⁻, 5%), 125 (100), and 81 (74).

Anal. Calcd. for C₂₀H₂₈O₃: C, 75.92, H, 8.92. Observed: C, 75.20, H, 8.61.

The isolated compound was identified by comparison with previously reported data (ir, pmr, ms, $[\alpha]$, mp) (5, 6), preparation of methyl hardwickiate, and comparison with an authentic specimen.

ISOLATION OF 1-TRIACONTANOL.—Fractions 40 to 80 (25 ml each) obtained from the previous silica gel 60 column were combined and evaporated under vacuum. Column chromatography of the residue (1.1 gm) on silica gel 60 (1.5 x 40 cm; 40 gm) with chloroform-ether (45:5) resulted in the concentration of the major component in fractions 18 to 26 (12 ml each). The compound was purified by crystallization from methanol, and was re-

crystallized twice from acetone to yield white flakes (57 mg), mp. 81° [lit. 85° (8)]; ir ν max (KBr) 3350, 1055 cm^{-1} ; pmr (CDCl_3 , 60 MHz) δ 3.66 (t, 2H, $J=6$ Hz), 1.88 (s, 1H), 1.56 (m, 2H), 1.26 (s, 54H), 0.96 (t, 3H); ms m/e 420 (M-18, 2.5%), 392 (3), 364 (1), 181 (6), 167 (8.5), 153 (12.5), 139 (18), 125 (38.5), 111 (50), 97 (79), 83 (80), 69 (77), 57 (100).

Anal. Calcd. for $\text{C}_{30}\text{H}_{52}\text{O}$: C, 82.11, H, 14.24. Observed: C, 82.07, H, 14.38.

The compound was identified by comparison with previously reported data (ms, ir, pmr, mp) (7, 8). No depression was observed with the mixed melting point of an authentic sample of 1-triacontanol.³

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³Analabs, Inc., North Haven, Connecticut.

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