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THE CO-OCCURRENCE OF DESMETHYLENCECALIN AND HYDROXYTREMETONE IN *EUPATORIUM RUGOSUM*

L. H. ZALKOW, L. GELBAUM, M. GHOSAL and T. J. FLEISCHMANN
School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332, U.S.A.

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Key Word Index—*Eupatorium rugosum*; Compositae; desmethylencecalin (7-hydroxy-2,2-dimethyl-6-acetyl-2H-chromene); hydroxytremetone (dehydroeuparin; 6-hydroxy-2-isopropenyl-5-acetylcumaranone).

Eupatorium rugosum (syn *E. urticaefolium*) was collected at Unicoi Gap, Appalachian Trail, Highway 75 north Georiga in September and October, 1976. Previous work on this plant includes the isolation and identification of tremetone, dehydrotremetone and hydroxytrometone [1]. The plant is responsible for 'milk sickness' in cattle and humans [1, 2]. Roots of freshly collected *E. rugosum*, in bloom, were macerated in 95% EtOH then continuously extracted with 95% EtOH to give 2% extract based on wet plant. Partition between 5% HCl and $CHCl_3$ yielded 16% of the extract in the organic layer, 43% of which was hexane soluble. GLC of the hexane soluble fraction showed five components (OV-17 column), the major component (~50%) being desmethylencecalin (1) and a minor component (~7%) having the same retention time alone and on admixture as authentic hydroxytremetone (2) on both OV-17 and SE-30 columns. Chromatography of the hexane soluble viscous oil on Si gel (230–400 mesh) and elution with hexane gave desmethylencecalin as orange crystals, mp 74–76°, rpt. [3] mp 77°, $\nu_{max}^{CCl_4}$ 3400–2500 (broad), 1645 cm^{-1}; δ (CCl_4) 1.39 (6H, *s*), 2.41 (3H, *s*), 4.50 (1H, *d*, J = 10 Hz), 6.21 (1H, *d*, J = 10 Hz), 6.21 (1H, *s*), 7.20 (1H, *s*), 12.44 (1H, *s*); MS: M^+ 218 (16%), 204 (100%), 202 (12%) 185 (10%). Identical with IR and ^{1}H NMR spectra of an authentic sample of desmethylencecalin [4].

Hydroxytremetone (2) was more readily isolated as follows. The EtOH extract (138 g) of the above ground portion of the green plant was steam-distilled and the aq. soln and insoluble portion were successively extracted with hexane, Et_2O and finally $CHCl_3$, then the aq. soln was filtered and evaporated to yield 91 g of residue. This residue was refluxed in 2N aq. EtOH–HCl, then extracted with Et_2O to give 15 g of residue which was refluxed in 10% ethanolic NaOH. Extraction of the latter solution with Et_2O (washing H_2O), drying and evaporation gave 0.7 g of residue which was chromatographed on Si gel (100–200 mesh) to give 190 mg of almost pure (2) in the hexane–EtOAc (4:1) eluent. Analytically pure (single peak by gas chromatography on SE-30 column) hydroxytremetone (2) was obtained by rechromatography on Si gel (100–200 mesh) and crystallization from hexane. Mp 63–65°, rpt. mp 70–71°, 69°; $[\alpha]_D^{25°}$ − 43° (*c*, 0.40, EtOH), rpt. $[\alpha]_D^{24°}$ − 50.7° (*c*, 0.74, EtOH); $\nu_{max}^{CCl_4}$ 1642: λ_{max} (EtOH) 208, 213, 232, 237, 280 and 335 nm; δ ($CDCl_3$) 1.75 (3H, *s*), 2.53 (3H, *s*), 2.95 (1H, *ddd*, J = 15, 9, 1), 3.29 (1H, *ddd*, J = 15, 9, 1), 4.93 (1H, *bs*), 5.07 (1H, *bs*), 5.26 (1H, *dd*, J = 9.9), 6.32 (1H, *s*), 7.48 (1H, *s*), 12.98 (1H, *s*); MS: Calc. for $C_{13}H_{14}O_3$: 218.0943, found, 218.0965; M^+ 218 (100), 203 (M^+-Me, 72%), 175 (M^+-MeCO, 42%). The UV, IR, ^{1}H-NMR and MS were identical, within experimental error, with the values reported in the literature and the IR and NMR spectra were identical, within experimental errors, to spectra of an authentic sample.

To our knowledge, the only prior report of the occurrence of desmethylencecalin has been in *Helianthella uniflora* where it co-occurs with hydroxytremetone [3]. Whereas hydroxytremetone has previously been reported in *E. rugosum* [1], its co-occurrence with desmethylencecalin is of particular phytochemical interest.

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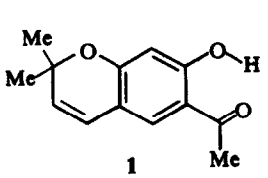

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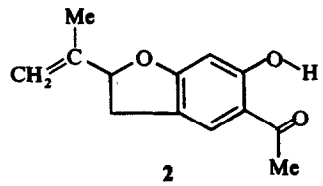

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