

OCCURRENCE OF (—)-*cis*-CHRYSANTHENYL ACETATE IN
CENTIPEDA CUNNINGHAMII

By J. T. PINHEY* and I. A. SOUTHWELL†

[Manuscript received February 24, 1971]

Centipeda cunninghamii (DC.) A.Br. & Aschers (family Compositae) is a native perennial semi-erect herb growing to a height of 30 cm. It occurs along the banks of dams and rivers, and in local depressions, in temperate regions of Australia. Growth and flowering take place in the warmer months as it is semi-dormant in winter.^{1,2} The plant is often referred to as "common sneezeweed" and "scentweed" because of its sternutatory and aromatic properties respectively. Late last century, this species, then grouped with other members of the same genus as *Myriogyne minuta*, was noted for its ability to relieve ophthalmia³ and was used by aborigines as a medicinal plant.⁴

Steam-distillation of the dried plant material collected near Barry, N.S.W., gave a low yield (0.2%) of a volatile oil. Examination of this material by infrared spectroscopy and gas-liquid chromatography indicated the presence of one major (45%) ester component, which could be isolated by fractional distillation.

Analysis of the ester indicated the formula $C_{12}H_{18}O_2$, while the spectral data suggested that it was an acetoxyl derivative of α -pinene (1; $X=Y=H$) or a closely related system. The nuclear magnetic resonance spectrum exhibited two three-proton singlets at δ 0.92 and 1.44, a three-proton quartet (J 2.0 Hz) at δ 1.68, and a broad one-proton multiplet at 5.24, which correspond approximately to the signals for the *gem*-dimethyl, C2 methyl, and C3 vinylic protons respectively of α -pinene.⁵ In support of such a structure, irradiation at δ 5.24 caused the vinylic methyl signal at δ 1.68 to collapse to a triplet (J 2.0 Hz, homoallylic coupling). Singlets at δ 2.08 (three protons) and 4.52 ($W_{h/2}$ 1.10 Hz) (one proton) were assigned to an acetoxyl group and the proton on the carbon bearing this group. Two broad two-proton multiplets at δ 2.15 and 2.33 accounted for the remaining signals. Assuming an α -pinene skeleton, the only position which the acetoxyl group could

* Department of Organic Chemistry, University of Sydney, N.S.W. 2006.

† Museum of Applied Arts and Sciences, Ultimo, N.S.W. 2007.

¹ Leigh, J. H., and Mulham, W. E., "Pastoral Plants of the Riverine Plain." p. 121. (Jacaranda Press: Melbourne 1965.)

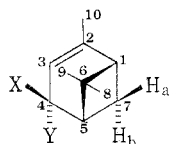
² Black, J. M., "Flora of South Australia." Revised by E. L. Robertson. Part 4, p. 882. (Govt. Printer: Adelaide 1957.)

³ Maiden, J. H., "Useful Native Plants of Australia." p. 195. (Trubner: London 1889.)

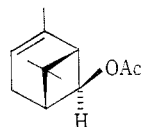
⁴ Smyth, R. B., "Aborigines of Victoria." Vol. 2, p. 173. (Trubner: London 1878.)

⁵ Varian Associates, "Nuclear Magnetic Resonance Spectra Catalog." Vol. 1, Spectrum 272. (Varian Associates: Palo Alto, Cal., 1962.)

occupy was C7. Attachment at C4 (verbenyl acetate) could be excluded, since, for both *cis*- (1; X = OH, Y = H) and *trans*- (1; X = H, Y = OH) verbenol, H4 shows a 3.0 Hz coupling to both H3 and H5.⁶ Of the two possible chrysanthenyl acetates, the *cis*-isomer (2) would be expected to display a singlet for H7, since models show that it makes a dihedral angle of approximately 90° with both H1 and H5. In keeping with this assignment, it has in fact been found for both *cis*- and *trans*-verbenol that there is no readily observable coupling between H1 and H7b, or between H5 and H7b, whereas H7a shows a small coupling (5–6 Hz) to both H1 and H5.



(1)



(2)

Confirmation that the ester was in fact (–)-*cis*-chrysanthenyl acetate and that it had the absolute stereochemistry displayed in (2) was readily obtained. Reduction of (2) with lithium aluminium hydride yielded (–)-*cis*-chrysanthenol, and this on oxidation with chromium trioxide–pyridine gave (+)chrysanthenone,⁷ which has the stereochemistry of (–)- α -pinene.⁸ This is the first reported occurrence of *cis*-chrysanthenyl acetate in nature. The synthesis of (+)-*cis*-chrysanthenyl acetate from (–)-chrysanthenone has recently been reported.⁹ A sample of this material, which was kindly supplied by Professor P. Teisseire, had a rotation (+32°) approximately equal to that of the natural ester (–30°). The synthetic (+)-*cis*-chrysanthenyl acetate and a sample of authentic chrysanthenone were found to be identical with the natural ester and the derived ketone respectively, by g.l.c. (two columns), infrared, and n.m.r. spectroscopy.

Although the alcohols and esters have not been found in nature previously, three occurrences of chrysanthenone have been reported.^{10–13}

Experimental

Optical rotations were determined in chloroform. Infrared spectra were measured as films on a Unicam SP 1200G spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian HA100 spectrometer in CDCl₃ with tetramethylsilane as internal reference. Gas chromatography was conducted with a Perkin–Elmer 226 gas chromatograph, using 140 ft by

⁶ Cooper, M. A., Salmon, J. R., Wittaker, D., and Scheidegger, U., *J. chem. Soc. (B)*, 1967, 1259.

⁷ Moscovitz, A., Mislow, K., Glass, M. A. W., and Djerassi, C., *J. Am. chem. Soc.*, 1962, **84**, 1945.

⁸ Hurst, J. J., and Whitham, G. H., *J. chem. Soc.*, 1960, 2864.

⁹ Teisseire, P., Rouillier, P., and Galfré, A., *Recherches (Paris)*, 1967, No. 16, 68.

¹⁰ De Pascual Teresa, P., Sanchez Bellido, H., and Sanchez Bellido, I., *An. R. Soc. esp. Fis. Quím. (B)*, 1962, **58**, 339.

¹¹ Kotake, M., and Nonaka, H., *Liebigs Ann.*, 1957, **607**, 153.

¹² Blanchard, E. P., *Chem. Ind.*, 1958, 293.

¹³ Penfold, A. R., Ramage, E. R., and Simonsen, J. L., *J. chem. Soc.*, 1939, 1496.

0.01 in. Gelay columns containing Castorwax or Apiezon L as the stationary phase, and helium as the carrier gas. Analyses were carried out by the Australian Microanalytical Service, Melbourne.

Isolation of (-)-cis-Chrysanthenyl Acetate from Centipeda cunninghamii

The dried plant material (2.65 kg) from Barry, N.S.W., was steam-distilled with cohobation in an all-glass apparatus, to yield a yellow oil (53 ml, n_D^{20} 1.4619, $[\alpha]_D^{18}$ -16.56° , d_4^{20} 0.9439). Fractional distillation of the oil (20 ml) yielded (-)-*cis*-chrysanthenyl acetate (2 ml, b.p. $84^\circ/8$ mm, n_D^{18} 1.4707, $[\alpha]_D^{20}$ -30.3° , d_4^{20} 0.9673), which gave a single peak on g.l.c. (Found: C, 74.3; H, 9.6. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%). ν_{\max} 1740, 1240, 1174, 1060, 1033, 791 cm^{-1} .

(-)-cis-Chrysanthenol

(-)-*cis*-Chrysanthenyl acetate (2.0 g) was added dropwise to a suspension of lithium aluminium hydride (0.25 g) in dry ether (150 ml). Further hydride was then added until hydrogen evolution had ceased. Excess reagent was decomposed by the dropwise addition of water and the organic layer washed with 2% sulphuric acid (250 ml). The ether solution yielded (-)-*cis*-chrysanthenol as a colourless oil (1.6 g, $[\alpha]_D^{20}$ -50.4°); single peak on g.l.c.; ν_{\max} 3320, 1263, 1175, 1070, 1031, 990, and 786 cm^{-1} . The n.m.r. spectrum showed singlets at δ 1.57 and 0.90 (each three protons, *gem*-dimethyl), and multiplets at δ 5.20 (one proton, vinylic), 3.96 (one proton, H 7, sharpened to a singlet on D_2O exchange), 2.40 (one proton, OH, exchanged with D_2O), 2.25 (two protons, H 4), 1.99 (two protons, H 1 and H 5), and 1.67 (three protons, H 10).

(+)-Chrysanthenone

Cornforth reagent¹⁴ was prepared by adding chromium trioxide (2.0 g) in water (2.0 ml) to pyridine (20 ml) with stirring and cooling. (-)-*cis*-Chrysanthenol (1.20 g) in pyridine (5.0 ml) was added to this mixture, which was kept at 0° with occasional shaking. After 4 hr, water (100 ml) was added and the mixture extracted with ether (2×50 ml). The ether extract, after washing with 2% sulphuric acid (4×100 ml), yielded crude (92% by g.l.c.) chrysanthenone (1.05 g), $[\alpha]_D^{20}$ $+69.5^\circ$, ν_{\max} 1788 cm^{-1} (identical with authentic material by g.l.c. and infrared spectrum). The n.m.r. spectrum displayed a singlet at δ 1.21 (six protons, *gem*-dimethyl) and multiplets at δ 5.35 (one proton, vinylic), 2.59 (four protons, H 4, H 1, and H 5), and 1.70 (three protons, H 10). Attempts to purify the ketone by column chromatography and preparative g.l.c. resulted in decomposition, as found by previous workers.⁹

Acknowledgments

We are indebted to Messrs R. Mendham and I. Mackenzie of Barry for assistance in collecting the plant material, and to Miss N. Ford, National Herbarium of New South Wales, for identifying the plant material. We also wish to thank Dr P. Schudel (Givaudan Esrolko) and Dr P. Teisseire (Roure Bertrand Fils & Justin Dupont) for samples of chrysanthenone and *cis*-chrysanthenyl acetate respectively, and Mr A. Hughes and Mrs B. Toyer for technical assistance.

¹⁴ Cornforth, R. H., Cornforth, J. W., and Popjak, G., *Tetrahedron*, 1962, **18**, 1351.