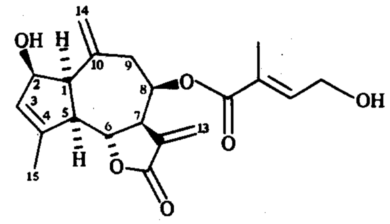

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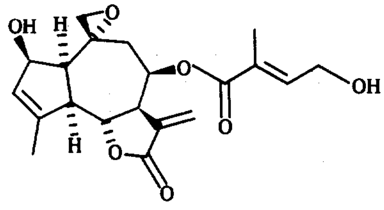

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# A GERMACRANOLIDE FROM *CYATHOCLINE LUTEA*

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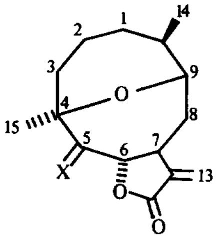
**Key Word Index**—*Cyathocline lutea*; *C. lyrata*; Compositae; Astereae; sesquiterpene lactones; germacranolides; 5$\beta$-hydroxy-4,9-oxidogermacr-11-en-6,12-olide.

**Abstract**—While *Cyathocline lyrata* only afforded known compounds, the aerial parts of *C. lutea* gave a new sesquiterpene lactone, 5$\beta$-hydroxy-4,9-oxidogermacr-11-en-6,12-olide.

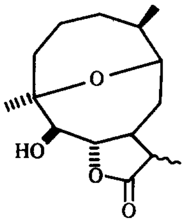
Two species of the small genus *Cyathocline* have been investigated chemically. While only the volatile compounds from *C. lyrata* D. Don have been studied so far [1, 2], *C. purpurea* Kuntze afforded a eudesmanolide and a guaianolide [3]. We have now studied again the aerial parts of *C. lyrata*. In addition to thymohydroquinone dimethyl ether, 10-isobutyryloxy-8,9-epoxythymol isobutyrate, parthenolide [4] and balchanin [5] were isolated.

The polar fractions of the aerial parts of *C. lutea* Cass. afforded a crystalline compound of molecular formula $C_{15}H_{22}O_4$; its IR and $^1H$ NMR spectra clearly showed the presence of a methylene lactone. Furthermore, a hydroxyl group was indicated by the IR band, as well as by the result of acetylation and oxidation, which led to the formation of a monoacetate and a ketone, respectively. Catalytic hydrogenation gave a dihydro derivative. While the signals at 60 and 90 MHz could only be partly assigned in the high-field $^1H$ NMR spectra of the natural compound and the corresponding acetate, most signals were well-resolved and were assigned by spin-decoupling (Table 1). Irradiation of the five-fold doublet at $\delta 3.03$ (H-7) in the spectrum of the acetate allowed the assignment of H-6–H-8 and H-13. Irradiation of the H-7 signal further allowed the assignment of the three-fold doublets of H-8, which were coupled with a three-fold doublet at $\delta 3.76$. The latter was coupled with a multiplet, its irradiation collapsing the methyl doublet at $\delta 0.93$ to a singlet. The multiplicity of the multiplet (H-10) followed from the spectrum of the corresponding acetate (Table 1), and required a neighbouring methylene group (H-1). The presence of an additional methyl group on an oxygen-bearing carbon followed from the methyl singlet at $\delta 1.28$, while the molecular formula required two more methylene groups and an oxygen bridge. The chemical shift differences of one of the low-field signals in the spectra of the carbinol and acetate clearly showed that the hydroxyl group was at C-5, and consequently the oxygen bridge was between C-4 and C-9, leading to the structure **1**. The stereochemistry was deduced from the coupling observed, and from inspection of a model, while the presence of a 6,12-lactone was supported by the negative Cotton effect in the CD spectrum of the acetate (**1**-Ac). The $^{13}C$ NMR signals also agreed with the proposed structure (see Experimental).

Sesquiterpene lactones are extremely rare in the tribe Astereae; only a few eudesmanolides with a 7,11-double bond have been reported from one *Aster* species [6]. A close relationship of *Cyathocline* to the tribe Inuleae could be proposed since no acetylenes have been isolated, from *Cyathocline*. Additionally, similar sesquiterpene lactones and thymol derivatives are common in the Inuleae. However, further investigations are needed to clarify the systematics of this tribe.



X
**1** β OH,H
**2** O



**3**

## EXPERIMENTAL

Cyathocline lutea. The air-dried plant material, collected from Lonawala (Maharashtra, India) during December 1979 (4 kg), was extracted with cold $Me_2CO$ for 24 hr at room temp., affording 200 g solid. 100 g was separated by CC (silica gel) with mixtures of $Me_2CO$–petrol. Repeated CC of the polar fractions ($Me_2CO$–petrol, 1:2) afforded 500 mg **1**, colourless crystals from EtOH, mp 136–138°, $[\alpha]_D^{30}$ +53.3°, $CHCl_3$, $c = 0.6$. IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 3300 (OH), 1760 (γ-lactone), 1660 (C=C); MS $m/z$ (rel. int.): 266.152 $[M]^+$ (7) ($C_{15}H_{22}O_4$), 248 $[M - H_2O]^+$ (7), 230 $[248 - H_2O]^+$ (7), 55 (100); $^{13}C$ NMR ($CDCl_3$) (C-1–C-15): 35.1 *t*, 30.9 *t*, 38.5 *t*,† 80.6 *s*, 74.5 *d*, 82.5 *d*,‡ 42.3 *d*, 39.1 *t*,† 82.7 *d*, ‡26.1 *d*, 140.3 *s*, 169.4 *s*, 119.0 *t*, 21.2 *q*, 21.8 *s* († and ‡ indicate signals which may be interchangeable). The compound gave an acetate (pyridine–$Ac_2O$) as a colourless gum. [Purity was controlled by TLC in different solvent mixtures (silica gel, $Et_2O$–petrol, 3:1; and $CHCl_3$–$C_6H_6$–$Et_2O$, 5:5:1) and by the $^1H$ NMR spectrum.] IR $\nu_{max}^{Nujol}$ cm$^{-1}$: 1760 (γ-lactone), 1720,

Table 1. $^1H$ NMR spectral data of compounds **1–3** ($CDCl_3$, TMS as internal standard)

| | **1*** | ($CDCl_3/C_6D_6$) | **1**-acetate | **2**† | **3** ($C_6D_6$)† |
|---|---|---|---|---|---|
| H-5 | 4.19 *br d* | 3.92 *d* | 5.54 *d* | — | 3.76 *d* |
| H-6 | 4.21 *dd* | 4.03 *dd* | 4.26 *dd* | 5.30 *d* | 3.76 *dd* |
| H-7 | 2.89 *ddddd* | 2.54 *ddddd* | 3.03 *ddddd* | 2.30 *m* | 1.98 *m* |
| H-8α | 2.14 *ddd* | 1.89 *ddd* | 2.18 *ddd* | ‡ | ‡ |
| H-8β | 1.67 *ddd* | 1.46 *ddd* | 1.51 *ddd* | ‡ | ‡ |
| H-9 | 3.76 *ddd* | 3.65 *ddd* | 3.78 *ddd* | 3.80 *m* | 3.30 *ddd* |
| H-10 | 1.75 *m* | 1.50 *m* | 1.89 *dddq* | ‡ | ‡ |
| H-13 | 6.18 *d* | 6.07 *s* | 6.18 *d* | 6.16 *d* | 0.92 *d* |
| H-13′ | 5.45 *d* | 5.20 *s* | 5.46 *d* | 5.46 *d* | |
| H-14 | 0.93 *d* | 0.80 *d* | 0.96 *d* | 0.86 *d* | 0.58 *d* |
| H-15 | 1.25 *s* | 1.23 *s* | 1.28 *s* | 1.33 *s* | 1.23 *s* |
| OAc | — | — | 2.12 *s* | — | — |
| OH | 2.65 *br s* | — | — | — | — |

*400 MHz.
†60 MHz.
‡Signals not resolved.
*J* (Hz): 1, 10 = 2; 1′, 10 = 10; 5, 6 = 9.5; 6, 7 = 9.5; 7, 8 = 4; 7, 8′ = 12; 8, 9′ = 13.5; 8, 9 = 2; 8′, 9 = 4.5; 9, 10 = 11; 7, 13 = 3; 7, 13′ = 3; 10, 14 = 6.

1240 (OAc); MS $m/z$ (rel. int.): 308 $[M]^+$ (17), 266 $[M - \text{ketene}]^+$ (15), 248 $[M - HOAc]^+$, (23), 230 $[248 - H_2O]^+$ (12), 55 (100); CD (MeCN) $\Delta_{\varepsilon 258} = -0.92$.

100 mg **1** in 5 ml $Me_2CO$ was stirred for 1 hr with 0.1 ml Jones reagent at room temp. Usual work-up gave 92 mg of a crystalline solid, mp 195–197° ($C_6H_6$); IR $\nu_{\max}^{\text{Nujol}}$ cm$^{-1}$: 1780 (γ-lactone), 1740 (C=O), 1660, 885 (C=C); MS $m/z$ (rel. int.): 264 $[M]^+$ (14), 220 $[M - CO_2]^+$ (40), 55 (100).

On hydrogenation in the presence of palladium on carbon (100 %), 100 mg **1** gave **3**, colourless crystals, mp 65–68°; IR $\nu_{\max}^{\text{Nujol}}$ cm$^{-1}$: 3450 (OH), 1780 (γ-lactone).

Cyathocline lyrata (*collected near Dehradun, India*). The air-dried aerial parts (200 g) were extracted with $Et_2O$–petrol (1:1) and the extract obtained was separated by CC (silica gel, 50 ml). The fractions with $Et_2O$–petrol (1:10) gave by TLC ($SiO_2$, PF 254, detection of the zones by UV light, 255 nm) 5 mg thymohydroquinone dimethyl ether ($R_f$, 0.65) and 10 mg 10-isobutyryloxy-8,9-epoxythymol isobutyrate ($R_f$, 0.55). Fraction with $Et_2O$ afforded on TLC (silica gel, $Et_2O$–petrol; 3:1) 20 mg parthenolide ($R_f$, 0.52) and 100 mg balchanin ($R_f$, 0.45). (All compounds were identified by comparing the 400 MHz $^1H$ NMR spectra with those of authentic material.)

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# CADINA-4,11-DIENE FROM *VIGUIERA OBLONGIFOLIA*

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**Key Word Index**—*Viguiera oblongifolia*; *V. lanceolata*; Compositae; sesquiterpenes; cadinane derivative; furanoheliangolides.

**Abstract**—*Viguiera oblongifolia* afforded two known furanoheliangolides and a new cadinane derivative whose structure was established by spectroscopic methods. From *V. lanceolata* 17,18-dihydrobudlein A was isolated.

Several species of the large genus *Viguiera* (tribe Heliantheae, subtribe Helianthinae) have been investigated chemically [1]. Most of them contain heliangolides, especially cytotoxic furanoheliangolides [1]. The aerial parts of *Viguiera oblongifolia* Gardn. afforded β-bisabolene, 7αH-silphiperfol-5-ene [2], dehydrofalcarinol, the furanoheliangolides atripliciolide angelate [3] and the corresponding 2-methyl butyrate [4] as well as a hydrocarbon, molecular formula $C_{15}H_{24}$ which appeared to be new. The $^1H$ NMR spectrum (Table 1) indicated the presence of two olefinic and one secondary methyl groups. Furthermore three olefinic protons must be assumed. The corresponding low field signals were coupled with the olefinic methyl groups and several allylic protons. The broadened singlet at $\delta = 2.55$ was due to one of the allylic protons. Spin decoupling made it possible to assign all signals and led to approximate coupling constants for those signals which overlapped. All data agreed with the presence of cadina-4,11-diene (**1**). The stereochemistry at

Table 1. $^1H$ NMR spectral data of compounds **1** in $CDCl_3$ (400 MHz, TMS as internal standard)

| | | | |
|---|---|---|---|
| H-1 | 1.77 *m* | H-8β | 1.24 *dddd* |
| H-2α | 1.56 *dddd* | H-9α | 0.96 *dddd* |
| H-2β | 1.32 *dddd* | H-9β | 1.67 *dddd* |
| H-3α | 1.98 *br d* | H-10 | 1.40 *dddq* |
| H-3β | 1.82 *br dd* | H-12 | 1.73 *dd* |
| H-5 | 5.50 *br s* | H-13 | 4.86 *ddq* |
| H-6 | 2.55 *br s* | H-13′ | 4.64 *br s* |
| H-7 | 1.95 *br d* | H-14 | 1.60 *br dd* |
| H-8α | 1.50 *ddddd* | H-15 | 0.87 *d* |

*J* (Hz): 1, 2α = 1, 2β = 2α, 3α = 2β, 3β = 6, 7 = 7, 8α = 8α, 9α = 8α, 9β = 8β, 9β ~ 3; 1, 10 = 2α, 2β = 2α, 3β = 3α, 3β = 7, 8β = 8α, 8β = 8β, 9α = 9α, 9β ~ 12; 3α, 5 = 3β, 5 = 3α, 6 = 3β, 6 = 3α, 14 = 5, 6 = 6, 8α = 7, 13 = 7, 13′ = 12, 13 = 13, 13′ ~ 1.5; 9α, 10 = 11; 10, 15 = 7.