gel (C_6H_6–hexane, 1:2) to give **1** (7.3 mg); MS *m/z* (rel. int.): 236 $[M]^+$ (17.2), 204 (23.7), 152 (100), 109 (37.1), 85 (37.1), 75 (47.8). Fractions B and C gave, on repeated chromatography on silica gel, bornyl acetate (11.5 mg) and farnesyl acetate (74 mg), respectively.

The Et_2O–hexane (1:2) eluate (12 g), on chromatography, followed by prep. TLC on silica gel gave farnesol (4.3 g), farnesal (0.5 g), manool (72.4 mg), α- and β-eudesmols (17.4 mg) and a resinous material which, after acetylation with Ac_2O in pyridine, was rechromatographed on silica gel to give acetates of abietinol (20.3 mg), dehydroabietinol (5.3 mg) and isopimarinol (9.9 mg).

The EtOAc eluate (2.6 g) was rechromatographed on silica gel (52 g), to give sitosterol (77 mg) and a resinous material which was subjected to HPLC (LiChroprep RP-8, H_2O–MeOH, 1:9), to give **2** (6.9 mg), 19-acetoxy-manool (9.5 mg) and torulosol (6.5 mg)

Syntheses of **1** *and* **2**. To a soln of β-eudesmol (222 mg) in MeOH (1 ml) was added $Hg(OAc)_2$ (319 mg) with stirring at room temp. After 90 min, 3 M NaOH (1 ml) and 0.5 M $NaBH_4$ in 3 M NaOH (1 ml) were added and stirred for 90 min. The reaction mixture was extracted with Et_2O (10 ml), and the Et_2O extract was washed with brine, dried and evapd, to give a crude product, which was chromatographed on silica gel (4.4 g, EtOAc–C_6H_6, 1:4) to give **2** (77.9 mg) and its epimer (32.0 mg). The synthesized **2** (25.2 mg) was dehydrated with $SOCl_2$ (0.1 ml) in C_6H_6 (5 ml) and pyridine (0.5 ml). The reaction mixture was washed with 5% HCl, brine and dried to give, on chromatography on 5% $AgNO_3$–silica gel (1 g, C_6H_6–hexane, 2:1), **1** (10.4 mg) and 4α-methoxy-selina-7-ene (3.2 mg).

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SESQUITERPENE LACTONES OF *CICHORIUM INTYBUS* AND *LEONTODON AUTUMNALIS**

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Key Word Index—*Cichorium intybus*; *Leontodon autumnalis*; *Sonchus oleraceus*; *S. arvensis*; *Hieracium pilosella*; Compositae; guaianolides; triterpenoids; Zimmermann rule.

Abstract—8-Deoxylactucin, lactucin and lactupicrin were isolated from *Cichorium intybus*. 8-Deoxylactucin and jacquilenin were isolated from *Leontodon autumnalis* and were found in particular abundance in flowers of the latter species. Flowers of *L. autumnalis* do not produce pentacyclic triterpenoid diols. Thus this species is the first noted exception to the Zimmermann rule, which correlates the co-occurrence of triterpenoid diols and carotenoids in flowers of Compositae plants.

Three closely related guaianolides, jacquilenin (**2a**), 8-deoxylactucin (**1a**) and lactucin (**3a**), were isolated as constituents of plants belonging to the tribe Cichorieae of the Compositae [1–4]. 8-Deoxylactucin is relatively active in the HeLa test (ED_{50} 0.26 μg/ml) especially when compared to lactucin, which shows much less activity (7.56 μg/ml) [5].

Cichorium intybus L., already known to produce lactucin [6] and lactupicrin [7], and *Leontodon autumnalis* L. were analysed and 8-deoxylactucin (**1a**) was isolated from both species. *L. autumnalis* contains only 8-deoxylactucin and jacquilenin, other lactones not being detected. Flowers of the latter species contain these lactones at tenfold the concentration of that in leaves and roots.

The extracts of *Sonchus oleraceus* L., *S. arvensis* L. and *Hieracium pilosella* L. (all collected in the Warsaw area,

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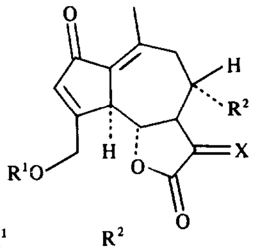
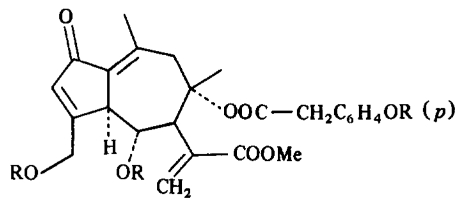
*Part 13 in the series "Terpenes of Compositae Plants"; presented at EUCHEM conference, Lago di Como, Italy (1977). For Part 12 see Pyrek, J. St. (1984) *J. Nat. Prod.* **47** (in press).



	R^1	R^2	X
1a	H	H	CH_2
1b	Ac	H	CH_2
2a	H	H	H, Me
2b	Ac	H	H, Me
3a	H	OH	CH_2
4a	H	$OOCCH_2C_6H_4OH(p)$	CH_2



5a R = H
5b R = Ac

Poland) were also studied but the above sesquiterpene lactones were not detected.

Extraction of fresh *C. intybus* plant in methanol is responsible for the formation of a detectable amount of the artefactual methyl ester derived from lactupicrin (**4a**). The NMR and mass spectral data (see Experimental) unequivocally indicated the structure **5a**. This substance was not detected in the extract prepared in acetone. The absence of the analogous products derived from the other three sesquiterpene lactones present in the extract points to the peculiar susceptibility of lactupicrin (**4a**) towards the lactone opening.

In the neutral fraction, obtained from the saponified extract of the flowers of *L. autumnalis*, the usual constituents of carotenoid-containing Compositae flowers—pentacyclic triterpenoid 3β,16β-dialcohols: maniladiol, coflodiol, faradiol, arnidiol and calenduladiol [8]—were not detected. Therefore this plant represents the first noted exception to the Zimmermann rule, which correlates the appearance of carotenoid pigments with the presence of these diols. All Compositae species investigated up to now were found to comply with this rule [9–11].

EXPERIMENTAL

Extraction of Cichorium intybus *L.* Whole, freshly collected plants (Warsaw area, Poland, 1977), divided into root (125 g) and aerial part (300 g), were blended in a ten-fold excess of either MeOH or Me_2CO. The extract was concd, dissolved in 50% MeOH, extracted with hexane (2 × 100 ml) and titrated with saturated lead diacetate until no more ppt. was formed. The soln was filtered the next day and extracted with $CHCl_3$ (5 × 25 ml) to give 131 mg (0.1%, the aerial part) and 226 mg (0.08%, root part) of the residue

HPLC analysis. Partisil-10 column, 30 × 0.6 cm and solvent mixture $CHCl_3$–hexane–MeOH (12:12:1) were used for the analytical separation monitored at 256 nm. The compositions of both extracts were similar: 8-deoxylactucin (**1a**) R_v = 12.2 ml, 30%, lactupicrin (**4a**) 32.6 ml, 50–52%, lactucin (**3a**) 43.4 ml, 11–16%; and lactupicrin methyl ester (**5a**) 63.6 ml, 4–6%, absent when Me_2CO was used for extraction of fresh plant.

8-Deoxylactucin (**1a**) was separated on a silica gel column (10 g) with a $CHCl_3$–Me_2CO gradient (5–50%, 300 ml) Mp 141–144° (from Et_2O–$CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3450, 1760, 1670, 1610, 1250, 1130, 990, 980. It was identified by direct comparison with the substance isolated previously from *Lactuca serriola* L [1] Lactucin (**3a**) and lactupicrin (**4a**), obtained from this separation, were also identical to the compounds isolated previously.

Lactupicrin methyl ester (**5a**) was isolated by the above chromatographic separation (only in the case of the MeOH extract) and purified by HPLC (non-crystalline solid). IR ν_{max}^{KBr} cm^{-1}: 1718, 1685, 1635, 1610, 1512; EIMS (15 eV, probe) *m/z* (rel int.): 442 $[M]^+$ (0.1), 424 $[M - H_2O]^+$ (0.3), 410 $[M - MeOH]^+$ (3.5), 258 (25), 229 (6), 152 (36), 107 (100); ^1H NMR (100 MHz, pyridine-d_5): δ7.0 (4 × aromatic H), 6.93 *br s* (H-3), 6.35 *br s* and 5.75 *br s* (CH_2-13), 3.75 *s* (CH_2 benzylic), 3.60 *s* (OMe), 2.48 *br s* (Me-15); (100 MHz, Me_2CO-d_6): δ6.85 *q* (4 × aromatic H), 6.27 *br s* (H-3), 6.08 *br s* and 5.63 *br s* (CH_2-13), 4.85 *d* and 4.35 *d* (*J* = 19 Hz, CH_2-14), 3.62 *s* (OMe), 3.30 *s* (CH_2 benzylic), 2.33 *br s* (Me-15) Triacetate (**5b**), ^1H NMR (100 MHz, pyridine-d_5): δ7.1 *q* (4 × aromatic H), 6.32 *br s* (H-3), 6.08 *br s* and 5.46 *br s* (CH_2), 5.0 *m* (H-6 and H-8), 4.72 *br s* (CH_2-14), 3.71 *s* (OMe), 3.50 *s* (CH_2 benzylic), 2.5–3.0 *m* (CH_2-9), 2.38 *br s* (Me-15), 2.28 *s*, 2.08 *s* and 1.95 *s* (3 × OAc).

Extraction of Leontodon autumnalis *L.* (a) Dry flowers (51 g, collected in Mazury lake district, Poland, 1977) were extracted with MeOH–CH_2Cl_2. The same procedure as described above (with the omission of lead diacetate precipitation) afforded a mixture of 8-deoxylactucin (**1a**) and jacquilenin (**2a**) (145 mg, 0.3%, dry wt). (b) Fresh whole plants (collected in Warsaw area, 1978), divided into leaves (80 g) and roots (18 g), were extracted and analysed as described for *C intybus*. Only jacquilenin (0.003%, fr wt) and 8-deoxylactucin (0.01%) were detected in both extracts. The mixture of sesquiterpenes was acetylated (pyridine–Ac_2O, room temp) and separated by prep. TLC (hexane–EtOAc, 3:2, 3 developments) to give **1b** and **2b**.

Jacquilenin acetate (**2b**) Mp 154–156° (from CH_2Cl_2–hexane, 21.5 mg); IR ν_{max} cm^{-1}: 1780, 1745, 1680, 1640, 1255, 1230, 1034, 1000, 885; ^1H NMR (100 MHz, $CDCl_3$): δ6.29 *br s* (H-3), 5.23 *dd* (*J* = 17 and 2 Hz) and 4.97 *dd* (*J* = 17 and 1 Hz, CH_2-14), 3.5–3.7 *m* (H-5, H-6), 2.43 *br s* (Me-15), 1.8–2.6 *m* (CH_2-9), 2.11 *s* (OAc), 1.2–1.6 *m* (CH_2-8), 1.25 *d* (*J* = 6.8 Hz, Me-13), (C_6D_6): 6.34 *br s* (H-3), 5.13 *br d* and 4.88 *br d* (*J* = 17.5 Hz, CH_2-14), 2.85 *br d* (*J* = 11 Hz, H-5), 2.56 *m* (H-6), 1.65 *s* (OAc), 0.90 *d* (*J* = 6.5 Hz, Me-13); identical to the lactone isolated before [1]

8-Deoxylactucin acetate (**1b**). Non-crystalline solid (61 mg); IR ν_{max}^{KBr} cm^{-1}: 1770, 1740, 1680, 1630, 1620, 1220, 1125, 985, ^1H NMR (100 MHz, $CDCl_3$). δ6.31 *br s* (H-3), 6.16 *d* and 5.48 *d* (*J* = 3 Hz, CH_2-13), 5.27 *dd* (*J* = 17.5 and 2 Hz) and 5.01 *dd* (*J* = 17.5 and 1 Hz, CH_2-14), 3.5–3.7 *m* (H-5, H-6), 2.89 *br* (H-7), 2.44 *br s* (Me-15), 2.2–2.6 *m* (CH_2-9), 2.13 *s* (OAc), 1.3–1.6 *m* (CH_2-8); identical to the substance described before [1].

Analysis of hexane extract. The hexane extract obtained from dry flowers of *L. autumnalis* (1.2 g) was saponified in boiling MeOH–KOH (50 ml/5 g, 5 hr under N_2). The neutral extract was examined by TLC (hexane–EtOAc, 4:1); only carotenoid pigments, sterols and triterpenoid monoalcohols were detected whereas triterpenoid diols were completely absent.

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ENT-NORAMBREINOLIDE FROM *SIDERITIS NUTANS*

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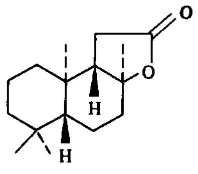
Key Word Index—*Sideritis nutans*; Labiateae; diterpenoid; *ent*-norambreinolide; X-ray analysis.

Abstract—*ent*-Norambreinolide has been isolated from *Sideritis nutans* and its structure determined by X-ray analysis.

Continuing with our work on the phytochemical study of the genus *Sideritis*, endemic to the Canary Islands [1], we describe here the X-ray structure determination of *ent*-norambreinolide (**1**), isolated from *Sideritis nutans* Svent.

This substance, molecular formula $C_{16}H_{26}O_2$, has IR absorptions characteristic of a lactone and two geminal methyl groups. Its ^1H NMR spectrum shows resonances typical of four methyls and of two hydrogens on a carbon allylic to a carbonyl group. In the mass spectrum, the molecular ion (*m/z* 250) readily loses a methyl group (*m/z* 235) or carbon dioxide (*m/z* 206). The loss of both gives a fragment at *m/z* 191. As only a small quantity of **1** was isolated, an X-ray analysis was carried out. Figure 1 shows its molecular structure. The absolute configuration was determined from the CD curve. *ent*-Norambreinolide in methanol exhibited a negative maximum at 215 nm characteristic of the structure **1**. Its enantiomer has a positive Cotton effect [2].

Compound **1** has not been obtained previously as a natural compound, but its enantiomer has been prepared synthetically by sclareol oxidation [3–5], by ozonization of 12α-hydroxy-13-epimanoyl oxide [6], and by degradation of a manoyloxide derivative [7].



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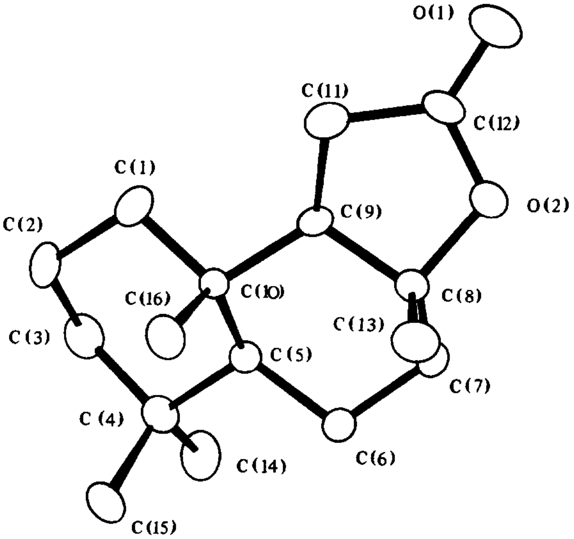

Fig 1. An ORTEP [10] drawing showing the relative molecular structure of *ent*-norambreinolide (**1**).