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# SESQUITERPENE LACTONES FROM *CENTAUREA SOLSTITIALIS*

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**Key Word Index**—*Centaurea solstitialis*; Compositae; yellow starthistle; sesquiterpene lactones; guaianolides; allelopathy.

**Abstract**—Eight sesquiterpene lactones were isolated from *Centaurea* solstitialis (yellow starthistle). They are solstitialin A, repin, subluteolide, acroptilin, janerin, cynaropicrin, and the new lactones solstitiolide and episolstitiolide.

## INTRODUCTION

Yellow starthistle (*Centaurea solstitialis* L.) is a major weed problem in the western United States and other parts of the world [1–3]. It aggressively invades cultivated fields, wastelands and rangelands and like other *Centaurea* sp., it is suspected to be allelopathic. In addition, it causes equine nigropallidal encephalomalacia (ENE) in horses, commonly called 'chewing disease' [4]. The specific toxin(s) causing ENE remain unidentified. However, the presence of sesquiterpene lactones in *Centaurea* sp. [5–15] and their known biological activity, e.g. cytotoxicity, phytotoxicity, etc. [16–18] led us to suspect similar toxic compounds as the causative agents of ENE and which may account for its suspected allelopathic behavior. Thus we have investigated the chemical composition of this plant in order to isolate and identify cytotoxic and phytotoxic substances.

*C. solstitialis* has been reported to contain alkaloids [19], triterpenes [20, 21], and the sesquiterpene lactones solstitialin A (**1a**) [5], solstitialin A 13-acetate (**1b**) [6], centaurepensin (**2a**) [8], scabiolide [7] and stizolicin [7]. In this paper, the presence of **1a** was confirmed. The compounds repin (**3a**), subluteolide (**3b**), acroptilin (**3c**), janerin (**3d**) and cynaropicrin (**4a**) were identified for the first time in *C. solstitialis*. In addition, two new lactones solstitiolide (**2b**) and episolstitiolide (**2c**) were isolated and their structures elaborated. Physical properties of compounds **3c**, **3d** and **4a** were identical to those of authentic samples previously isolated in this laboratory from *Centaurea repens* L. [9, 22]. The structures of solstitialin A (**1a**), centaurepensin (**2a**) and acroptilin (**3c**) had been previously determined by X-ray crystallography [5, 22, 23]. Repin (**3a**) has been correlated with **2a** and **3c** [13] and cynaropicrin (**4a**) has been correlated with α-santonin [24].

## RESULTS AND DISCUSSION

The major sesquiterpene lactone (0.05%) of *C. solstitialis* was solstitialin A (**1a**). We observed a higher melting point (215–217°) than the reported value (206–207°) [5] and comparison of our $^1$H NMR spectrum with those in the literature [5, 15] showed slight discrepancies*. To establish unequivocally the structure of **1a**, a series of decoupling experiments was performed on the spectrum of **1a** and acetyl derivatives **1a–e** were prepared. $^1$H NMR spectral assignments (Table 1) were consistent with structures **1a–1e**.

$^{13}$C NMR chemical shifts (Table 2) for **1a–e** were obtained using a multiplicity separation pulse sequence [25], which aided assignments of the signals. Comparison of the spectra of **1c** and **1e** with those of **1b** and **1d** showed the *ipso* carbon signal (C-3) to have shifted 2 ppm downfield upon acetylation, the two carbon signals (C-2 and C-4) shifted upfield, and the γ-carbon signal (C-15) shifted downfield consistent with acetylation of the C-3 hydroxyl. Acetylation of the tertiary hydroxyl at C-11 (**1d** and **1e** *vs* **1b** and **1c**) caused a similar shift downfield of the *ipso* carbon signal (C-11) and upfield shifts of the three β-carbon signals (C-7, C-12 and C-13). Assignments for the other carbons are comparable to those of dehydrocostus lactone (**4b**) [26], cynaratriol (the 4,15-dihydro of **1a**) [27], and similar compounds [8, 28, 29]. $^{13}$C NMR spectral assignments hence confirmed the structures of solstitialin A (**1a**) and its acetates **1b–e**.

The diasteriomers repin (**3a**) and subluteolide (**3b**) were obtained as mixture A, and could not be separated. This is the first report of the two lactones occurring in the same plant. Repin (**3a**) and subluteolide (**3b**) have been reported [10, 13, 30] to have the same structure. The $^1$H NMR spectra of A and authentic **3a** (obtained from *C. repens*) [9] are very similar, except some of the signals for A are either slightly broadened or appear as discrete sets of signals with a ratio of 2:3. One set of peaks in the 200 MHz $^1$H NMR spectrum of A is identical to that of **3a** [9, 10, 13], while the other set is identical to the published spectrum of subluteolide (**3b**) [30]. Chemical shifts are virtually identical (Table 3), except for H-13 (δ5.56 *vs* 5.73), H-8 (δ5.14 *vs* 5.04), and H-9 (δ2.73 *vs* 2.79). Stevens [9] has proposed that the lactones **3a** and **3b** are epimeric at C-17. Indeed, Dreiding models indicate that a change of stereochemistry at C-17 would have the greatest steric and anisotropic effects at H-13, H-8 and H-9, and Stevens' proposal predicted the observed differences in chemical shifts noted above. In addition, the proposal accounts for the observed similarities of physical properties, providing an explanation for the failure to

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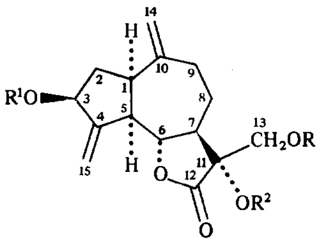
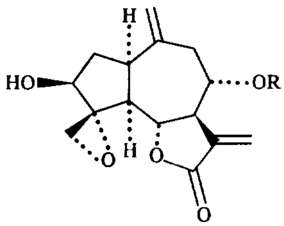
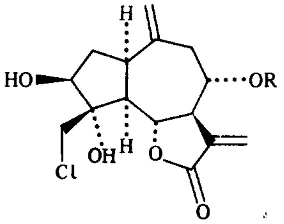
*The presence of water or other impurities in the original sample may account for the differences observed.



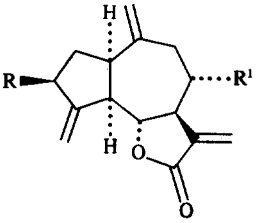
| | R | R¹ | R² |
|---|---|---|---|
| **1a** | H | H | H |
| **1b** | Ac | H | H |
| **1c** | Ac | Ac | H |
| **1d** | Ac | H | Ac |
| **1e** | Ac | Ac | Ac |



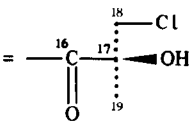
**3a** R = B
**3b** R = C
**3c** R = A
**3d** R = D



**2a** R = A
**2b** R = B
**2c** R = C



**4a** R = OH; R¹ = OD
**4b** R = R¹ = H

A =


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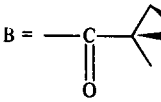

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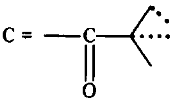

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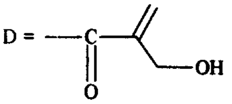

separate **3a** from **3b** and the confusion in the literature.

Two new sesquiterpene lactones **2b** and **2c** were also obtained as an intractable mixture **B**. Chemical ionization mass spectrometry showed two protonated molecular ion peaks at *m/z* 401 and 399 indicating the presence of a chlorine atom. These peaks formally correspond to the protonated molecular ions of **3a** or **3b** plus hydrogen chloride, or $[C_{19}H_{24}O_7Cl]^+$. The fact that two exocyclic methylenes are present in **2b** and **2c** at C-10 and C-11 ($^1$H NMR, Table 3) suggests that the difference between **3a** and **2b** may involve an epoxide *vs* a chlorohydrin. Acroptilin (**3c**) is the 17,18-epichlorohydrin of **3a**, but comparison of its physical properties (mp, NMR, IR, MS and TLC) with those of **B** indicates that **3c** is not a component of mixture **B**. Thus, it is likely that the chlorohydrin is at the 4,15-position. Indeed, both mixtures **A** and **B** readily lose 102 mass units in CIMS and have essentially identical NMR chemical shifts for H-18a, H-18b and H-19 (Table 3), demonstrating that each mixture has an epoxymethacrylate side chain. Furthermore, a downfield shift of the signals for H-15a (**A** *vs* **B**, δ3.07 *vs* 3.95) and H-15b (δ3.31 *vs* 4.32) was observed and is consistent with the conversion of the 4,15-epoxide in **A** and the epichlorohydrin in **B**. Similar chemical shifts have been reported for guaianolides having a 4,15-epichlorohydrin [8, 13, 31]. The chemical shifts in the $^1$H NMR spectra of **2b** and **2c** are very similar with the exception of the signals of H-8, H-9 and H-13 and, as in the spectra of **3a** and **3b**, suggest that **2b** and **2c** are C-17 epimers. We propose the names solstitiolide (for repin 4,15-chlorohydrin, **2b**) and episolstiolide (for subluteolide 4,15-chlorohydrin, **2c**).

$^{13}$C NMR spectra of several guaianolides in pyridine-$d_5$ are being reported elsewhere [31]. We include here the spectra of **3a**, **3b**, **3c**, **2b** and **2c** (Table 4) to show that the structures proposed for **2b** and **2c** are consistent with their spectra. It was found empirically that a discrete set of resonances are associated with each kind of ester side chain and with each type of 5-membered carbocyclic ring. For example, the 5-membered carbocyclic ring in **3a–d** has resonances at δ39.0 ± 0.2 (C-2), 75.5 ± 0.1 (C-3), 69.3 ± 0.2 (C-4), 53.0 ± 0.3 (C-5), and 48.7 ± 0.3 (C-15), whereas the

Table 1. $^1H$ NMR spectra of solstitialin (**1a**) and its acetates (**1b–e**) in pyridine-$d_5$

| | **1a***  | **1b** | **1c** | **1d** | **1e** |
|---|---|---|---|---|---|
| H-1 | 2.90 *m* | 2.88 *ddd* | 2.86 *ddd* | 2.83 *ddd* | 2.83 *ddd* |
| H-2a | 2.40 *dt* | 2.38 *dt* | 2.50 *dt* | 2.35 *dt* | 2.44 *dt* |
| H-2b | 2.00 *ddd* | 2.00 *ddd* | 1.80 *ddd* | | 1.86 *ddd* |
| H-3 | 4.83 *ddd* | 4.83 *dd* | 5.74 *dd* | 4.78 *dd* | 5.72 *dd* |
| H-5 | 2.90 *m* | 2.88 *ddt* | 2.86 *m* | 3.18 *ddt* | 3.17 *ddt* |
| H-6 | 4.90 *t* | 4.53 *t* | 4.43 *t* | 4.53 *t* | 4.95 *t* |
| H-7 | 2.82 *m* | 2.82 *ddd* | 2.81 *ddd* | 3.34 *ddd* | 3.32 *ddd* |
| H-8a | 2.37 *m* | 2.25 *m* | 2.25 *m* | | |
| H-8b | 2.17 *ddd* | 1.57 *ddd* | 1.54 *ddd* | 1.53 *ddd* | 1.52 *ddd* |
| H-9a | 2.59 *dt* | 2.52 *dt* | 2.50 *m* | 2.46 *dt* | 2.42 *m* |
| H-9b | 2.12 *m* | 2.02 *m* | *br* | *br* | *br* |
| H-13a | 4.28 *dd* | 4.69 *d* | 4.70 *d* | 4.63 *d* | 4.61 *d* |
| H-14a | 4.93 *s br* | 4.95 *s* | 4.93 *s* | 4.94 *s* | 4.94 *s* |
| H-14b | 5.09 *s br* | 5.13 *s* | 4.98 *s* | 5.14 *s* | 4.98 *s* |
| H-15a | 5.65 *m* | 5.61 *m* | 5.42 *m* | 5.61 *m* | 5.39 *m* |
| Ac | | | 2.07 *s* | | 2.06 *s* |
| Ac | | | | 2.06 *s* | 2.05 *s* |
| Ac | | 1.86 *s* | 1.90 *s* | 1.97 *s* | 1.99 *s* |

*Data from decoupling experiment at room temp. At 80°, H-7 moves upfield to 2.74 (*ddd*).

*J* (Hz): 1, 2a = 8; 1, 2b = 8.5; 1, 5 = 9; 2a, 2b = 14; 2a, 3 = 8; 2b, 3 = 6; 5, 6 = 9.5; 7, 8a = 3.5; 7, 8b = 12.5; 8a, 8b = 12; 8a, 9b = 5; 9a, 9b = 12; 13a, 13b = 11; 5, 15a = 2.5; 3, OH = 5; 13, OH = 5.

Table 2. $^{13}C$ NMR spectra of sesquiterpene lactones **1a–e**

| | **1a*** | **1b*** | **1b†** | **1c†** | **1d†** | **1e†** |
|---|---|---|---|---|---|---|
| C-1 | 42.0 | 42.0 | 43.0 | 43.5 | 43.5 | 43.9 |
| C-2 | 38.0 | 37.9 | 38.3 | 36.1‡ | 38.7 | 36.2‡ |
| C-3 | 71.6 | 71.6 | 73.3 | 74.6 | 73.5 | 74.7 |
| C-4 | 154.3 | 153.9 | 152.4 | 147.5§ | 152.8 | 148.0 |
| C-5 | 51.6 | 51.6 | 52.5 | 52.1 | 49.8 | 50.1 |
| C-6 | 81.5 | 81.3 | 82.0 | 81.8 | 82.7 | 82.5 |
| C-7 | 49.1 | 48.8 | 49.7 | 50.1 | 46.6 | 46.3 |
| C-8 | 26.0 | 26.5 | 26.8 | 26.8 | 26.6 | 26.8 |
| C-9 | 36.2 | 35.8 | 35.9 | 35.9‡ | 35.5 | 35.7‡ |
| C-10 | 149.8 | 149.6 | 148.6 | 148.5§ | 148.1 | 148.0 |
| C-11 | 76.8 | 74.9 | 75.5 | 75.5 | 79.8 | 79.7 |
| C-12 | 178.6 | 176.4 | 176.5 | 176.2 | 171.9 | 171.7 |
| C-13 | 63.2 | 63.7 | 64.0 | 64.1 | 62.8 | 62.8 |
| C-14 | 112.2 | 112.4 | 113.6 | 113.7‖ | 114.1 | 113.9‖ |
| C-15 | 107.5 | 107.9 | 111.3 | 113.5‖ | 111.1 | 113.5‖ |
| $\underline{C}OCH_3$ | | 169.3 | 170.4 | 170.7 | 169.4 | 170.5 |
| $\underline{C}OCH_3$ | | | | 170.2 | 169.1 | 169.3 |
| $\underline{C}OCH_3$ | | | | | | 169.0 |
| $CO\underline{C}H_3$ | | 20.4 | 20.6 | 21.1 | 21.0 | 21.2 |
| $CO\underline{C}H_3$ | | | | 20.5 | 20.6 | 20.9 |
| $CO\underline{C}H_3$ | | | | | | 20.5 |

*In DMSO-$d_6$.

†In $CDCl_3$.

‡§‖Values with same superscript can be interchanged.

ring in **2a–c** has signals at δ40.3 ± 0.1 (C-2), 76.4 ± 0.1 (C-3), 85.4 ± 0.1 (C-4), 59.6 ± 0.2 (C-5) and 51.3 ± 0.1 (C-15). Likewise, an epoxymethacrylate side chain (as in **2b**, **2c**, **3a**, **3b**) can be described by signals at δ170.3 ± 0.2 (C-16), 54.3 ± 0.1 (C-17), 53.0 ± 0.1 (C-18) and 17.5 ± 0.1 (C-19), and its corresponding chlorohydrin (as in **2a**, **3a**) is delineated by resonances at δ173.4 ± 0.1 (C-16), 75.5 ± 0.1 (C-17), 52.1 ± 0.2 (C-18) and 24.4 ± 0.1 (C-19).

Table 3. $^1$H NMR spectra of sesquiterpene lactones **2b**, **2c**, **3a** and **3b** in $CDCl_3$

| | **2b** | **2c** | **3a** | **3b** |
|---|---|---|---|---|
| H-1 | 3.6 *m br* | 3.6 *m br* | 3.33* *m br* | 3.33* *m br* |
| H-2a | | | 1.81 *ddd* | 1.82 *ddd* |
| H-2b | | | 2.44 *ddd* | 2.47 *ddd* |
| H-3 | 4.17 *d br* | 4.17 *d br* | 3.98 *br* | 3.98 *br* |
| H-5 | | | 2.06 *dd* | 2.08 *dd* |
| H-6 | 4.74 *dd* | 4.72 *dd* | 4.63 *dd* | 4.62 *dd* |
| H-7 | 3.13 *m* | 3.13 *m* | 3.08† *m* | 3.08† *m* |
| H-8 | 5.13 *ddd* | 5.02 *ddd* | 5.14‡ *ddd* | 5.04 *ddd* |
| H-9a | | | 2.38 *d br* | 2.38 *d br* |
| H-9b | 2.71 *dd* | 2.64 *dd* | 2.73 *br* | 2.79 *dd* |
| H-13a | 5.59 *d* | 5.75 *d* | 5.56 *d* | 5.73 *d* |
| H-13b | 6.22 *d* | 6.24 *d* | 6.22 *d* | 6.23 *d* |
| H-14a | 4.86 *d* | 4.80 *d* | 4.97 *d* | 4.94 *d* |
| H-14b | 5.14 *s br* | 5.15 *s br* | 5.20 *s br* | 5.20 *s br* |
| H-15a | 3.95 *d* | 3.94 *d* | 3.07 *d* | 3.07 *d* |
| H-15b | 4.32 *d* | 4.32 *d* | 3.31 *d* | 3.31 *d* |
| H-18a | 2.83 *d* | 2.84 *d* | 2.83 *d* | 2.84 *d* |
| H-18b | 3.18 *d br* | 3.18 *d br* | 3.16 *d* | 3.20 *d* |
| H-19 | 1.62 *s br* | 1.62 *s br* | 1.62 *s br* | 1.62 *s br* |

*† Values given may differ from lit. values, since peaks are complex multiplets and under H-15a and H-15b peaks.

‡ Partially under H-14a peak.

*J* (Hz) for **2b** and **2c**: 7, 8 = 9.5; 7, 13a = 3.5; 7, 13b = 3.5; 8, 9a = 5; 8, 9b = 2; 9, 9 = 15; 15a, 15b = 12; 18a, 18b = 6.

Table 4. $^{13}$C NMR spectra of sesquiterpene lactones **2b–c** and **3a–c** in pyridine-$d_5$*

| | **2b** | **2c** | **3a** | **3b** | **3c** |
|---|---|---|---|---|---|
| C-1 | 46.5 | 46.3 | 46.0 | 45.8 | 46.1 |
| C-2 | 40.3 | 40.3 | 38.9 | 38.8 | 39.0 |
| C-3 | 76.4 | 76.4 | 75.5 | 75.5 | 75.4 |
| C-4 | 85.4 | 85.3 | 69.2 | 69.2 | 69.2 |
| C-5 | 59.5 | 59.5 | 53.1 | 52.7 | 53.3 |
| C-6 | 77.5 | 77.4 | 77.5 | 77.4 | 77.3 |
| C-7 | 48.6 | 48.6 | 47.8 | 47.6 | 47.7 |
| C-8 | 75.6 | 75.6 | 75.3 | 75.1 | 75.3 |
| C-9 | 35.0 | 35.1 | 36.4 | 36.9 | 36.2 |
| C-10 | 144.4 | 144.8 | 142.7 | 143.1 | 142.9 |
| C-11 | 138.9 | 138.7 | 138.6 | 138.2 | 138.6 |
| C-12 | 169.0 | 169.1 | 169.1 | 169.2 | 169.0 |
| C-13 | 120.8 | 121.6 | 121.1 | 122.0 | 121.4 |
| C-14 | 117.0 | 116.9 | 118.0 | 117.9 | 118.1 |
| C-15 | 51.2 | 51.2 | 48.6 | 48.5 | 48.5 |
| C-16 | 170.3 | 170.5 | 170.2 | 170.4 | 173.3 |
| C-17 | 54.4 | 54.3 | 54.3 | 54.2 | 75.4 |
| C-18 | 53.0 | 53.1 | 52.9 | 53.0 | 52.0 |
| C-19 | 17.6 | 17.5 | 17.5 | 17.4 | 24.3 |

*From ref. [32].

Compounds **2b** and **2c** have the resonances required for the structures proposed.

We have found guaianolides **1a**, **2a–c**, **3a–d** and **4a** to have an effect upon the radicle growth of lettuce seedlings similar to that of an auxin, although they seem to have no effect upon hypocotyl growth [31]. These compounds could thus be used by yellow starthistle as plant growth promotors for itself while simultaneously limiting or regulating the growth of other plants. Additional testing is necessary to prove this hypothesis.

Cynaropicrin (**4a**) has been reported to be cytotoxic ($LD_{50}$ 5 μg/ml) to He La cells [32] and centaurepensin (**2a**) toxic to 9 KB (human nasopharynx carcinoma, $ED_{50}$ 1.7 μg/ml) [8], but the low levels found in the plant make it unlikely that they are the sole cause of ENE. Therefore, tests for biological activity of the lactones described above in laboratory animals and plants are currently being undertaken. Rodriguez *et al.* [17] have observed that increased oxidation of sesquiterpene lactones increased their toxicity. The presence of a number of quite oxygenated guaianolides in yellow starthistle, *viz.* epoxides and epichlorohydrins, may be significant in the toxicity of this weed toward horses.

## EXPERIMENTAL

All mps are uncorr.; all $^1$H NMR spectra were recorded on a Nicolet superconducting 200 MHz spectrometer. $^{13}$C NMR were measured on Jeol PFT-100 operating at 22.05 MHz using a multiplicity pulse sequence [25] with a 90° flip angle at a 2 sec repetition rate. Quarternary carbons were identified using a 30° flip angle at a 2 sec repetition rate. TMS was used as internal standard. Above ground plant material was collected in 1980 along Marsh Creek Rd about 3 miles W of Camino Diablo Rd, Contra Costa County, California. A voucher specimen is deposited at the University of California Herbarium, Berkeley, CA.

*Extraction and isolation.* The air dried, ground material was extracted sequentially with petrol and $Et_2O$. The $Et_2O$ extract was concd, redissolved in EtOH, treated with aq. 4% PbOAc and filtered. After removal of EtOH, the filtrate was extracted with $CHCl_3$ and EtOAc. Concn of the EtOAc soln to a ppt gave upon recrystallization from MeOH–EtOAc solstitialin A (**1a**) (*ca* 0.05%). Acroptilin (**3c**), cynaropicrin (**4a**), janerin (**2d**), mixture A [repin (**3a**) and subluteolide (**3b**)], and mixture B solstitiolide (**2b**) and episolstitiolide (**222c**)] were obtained from the $CHCl_3$ extract by a combination of column chromatography (CC) and preparative TLC on silica gel using a variety of solvents (e.g. 1:1 $C_6H_6$–$Me_2CO$; 5:1 petrol–$Et_2O$; 9:1 $CHCl_3$–MeOH; 9:1 petrol–EtOAc, etc.). Spots were visualized on TLC by UV and by spraying with 2% aq. $KMnO_4$.

*Solstitialin A* (**1a**) was obtained as a colorless solid, mp 215–217° (lit. [5] mp 206–207°); IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3575, 3350, 3485 (OH), 1740 br (CO), 1660, 1640, 1235; 1235; $^1$H NMR and $^{13}$C NMR: Tables 1 and 2; CIMS (*i*-butane) *m/z* (rel. int.): 281 $[M+1]^+$ (53), 263 $[M+1-H_2O]^+$ (100), 245 $[M+1-2H_2O]^+$ (90), 235 (63), 217 (42), 159 (49).

*Solstitialin A 13-acetate* (**1b**). Compound **1a** (200 mg) was treated with $Ac_2O$ (73 mg) in pyridine (5 ml) overnight at 5–10°. Standard work-up and CC (silica gel, $CHCl_3$–$Me_2CO$, 7:3) gave as major product **1b** (142 mg), viscous oil; IR $\nu_{max}^{neat}$ cm$^{-1}$: 3450 (OH), 1780, 1750 (CO), 1640, 1235; $^{13}$C NMR: Table 2; CIMS (*i*-butane) *m/z* (rel. int.): 323 $[M+1]^+$ (3), 305 $[M+1-H_2O]^+$ (23), 277 (100), 217 (53); $^1$H NMR ($C_5D_5N$): Table 1; ($CDCl_3$): δ5.36 (*t*, $J = 2.5$ Hz, H-15), 5.35 (*t*, $J = 2.5$ Hz), 4.97 (*s*, H-14), 4.95 (*s*, H-14), 4.55 (*m*, H-3), 4.32 (*d*, $J = 11$ Hz, H-13), 4.16 (*t*, $J = 9.5$ Hz, H-6), 4.11 (*d*, $J = 11$ Hz, H-13), 2.88 (*m*, H-1), 2.58 (*m*, H-9), 2.48 (*m*, H-7), 2.44 (*m*, H-2), 2.07 (3H, *s*, OAc), 1.98 (*m*, 8a), 1.38 (*m*, H-8b).

*Solstitialin A* 3,11,13-*triacetate* (**1e**). Compound **1a** (200 mg) was stirred with excess $Ac_2O$ in pyridine overnight at 5–10°. Workup and CC ($CHCl_3$-$Me_2CO$, 9:1) gave **1e**, a viscous oil;

IR $\nu_{max}^{neat}$ cm$^{-1}$: 1785, 1740 (CO), 1640, 1215; $^{13}$C NMR (Table 2); CIMS (*i*-butane), *m/z* (rel. int.): 407 $[M+1]^+$ (13), 347 $[M+1-HOAc]^+$ (67), 287 $[M+1-2HOAc]^+$ (100), 229 (39); $^1$H NMR (pyridine-$d_5$: Table 1; (CDCl$_3$): $\delta$5.57 (*m*, H-3), 5.48 (*t*, $J = 5$ Hz, H-15), 4.96 (2H, *s br*, H-14), 4.40 (*d*, $J = 11$ Hz, H-13), 4.26 (*d*, $J = 11$ Hz, H-13), 4.13 (*t*, $J = 9.5$ Hz, H-6), 3.00 (*m*, H-5), 2.99 (*m*, H-7), 2.92 (*m*, H-1), 2.54 (*m*, H-9), 2.46 (*m*, H-2), 2.15 (3H, *s*, OAc), 2.12 (3H, *s*, OAc), 2.08 (3H, *s*, OAc), 1.80 (*ddd*, $J = 12, 8, 7$ Hz, H-2), 1.45 (*tdd*, $J = 12, 5, 2.5$ Hz, H-8).

*Solstitialin A* 3,13-*diacetate* (**1c**) *and* 11,13-*diacetate* (**1d**). Compound **1a** (1.0 g) was treated with Ac$_2$O (0.73 g) and excess pyridine as above. Work-up, repeated CC and preparative TLC gave **1c** (692 mg) and **1d** (170 mg), along with some **1b** (20 mg) and **1e** (45 mg). Compound **1c** was a viscous oil; IR $\nu_{max}^{neat}$ cm$^{-1}$: 3480 (OH), 1780, 1740, (CO), 1685, 1235; $^{13}$C NMR: Table 2; CIMS (*i*-butane) *m/z* (rel. int.): 365 $[M+1]^+$ (8), 305 $[M+1-HOAc]^+$ (100), 287 $[M+1-HOAc-H_2O]^+$ (21), 277 $[M+1-HOAc-CO]^+$ (87), 227 $[M+1-2HOAc-H_2O]^+$ (63); $^1$H NMR: Table 1; (CDCl$_3$): $\delta$5.56 (*m*, H-3), 5.42 (*t*, $J = 2.5$ Hz, H-15), 5.32 (*t*, $J = 2.5$ Hz, H-15), 4.97 (*s*, H-14), 4.93 (*s*, H-14), 4.32 (*d*, $J = 11$ Hz, H-13), 4.13 (*t*, $J = 9.5$ Hz, H-6), 2.92 (*m*, H-1), 2.90 (*m*, H-5), 2.58 (*m*, H-9), 2.48 (*m*, H-7), 2.12 (3H, *s*, OAc), 2.08 (3H, *s*, OAc), 1.40 (*m*, H-8). Compound **1d** was a colorless viscous oil; IR $\nu_{max}^{neat}$ cm$^{-1}$: 3500 (OH), 1790, 1745 (CO), 1680, 1640, 1220; $^{13}$C NMR: Table 2; CIMS (*i*-butane) *m/z* (rel. int.): 365 $[M+1]^+$ (12), 305 $[M+1-HOAc]^+$ (37), 287 $[M+1-HOAc-H_2O]^+$ (100), 277 $[M+1-HOAc-CO]^+$ (17), 227 $[M+1-2HOAc-H_2O]^+$ (19), 61 (36); $^1$H NMR pyridine-$d_5$: Table 1; (CDCl$_3$): $\delta$5.44 (*t*, $J = 2.5$ Hz, H-15), 5.33 (*t*, $J = 2.5$ Hz, H-15), 5.01 (*s*, H-14), 4.94 (*s*, H-14), 4.57 (*ddd*, $J = 7, 8, 2$ Hz, H-1), 4.38 (*d*, $J = 11$ Hz, H-13), 4.24 (*d*, $J = 11$ Hz, H-13), 4.16 (*t*, $J = 9.5$ Hz, H-6), 2.98 (*m*, H-5), 2.96 (*m*, H-7), 2.86 (*m*, H-1), 2.54 (*m*, H-9), 2.42 (*m*, H-2), 2.12 (3H, *s*, OAc), 2.06 (3H, *s*, OAc), 1.80 (*m*, H-2), 1.42 (*m*, H-8).

*Acroptilin* (**3c**). The amorphous solid obtained from CC was recrystallized several times from MeOH and seeded with authentic sample to give pure **3c**, mp 197–199° (mp [33] 196–198°); $^{13}$C NMR: Table 4; IR $\nu_{max}^{KBr}$ and $^1$H NMR (Me$_2$CO-$d_6$, pyridine-$d_5$) superimposable with those of authentic material [22].

*Janerin* (**3d**) *and cynaropicrin* (**4a**) were viscous oils. IR $\nu_{max}^{neat}$ and $^1$H NMR (CDCl$_3$, pyridine-$d_5$) and $R_f$ on TLC were identical to those of authentic materials [9].

*Repin* (**3a**) *and subluteolide* (**3b**) (mixture **A**) was obtained as a viscous oil, inseparable by HPLC, CC and TLC using a variety of solvent systems; in all solvents used the $R_f$ was identical to that of authentic repin (**3a**) [9]; $^1$H NMR (Table 3); $^{13}$C NMR: Table 4; CIMS (*i*-butane) *m/z* (rel. int.): 363 $[M+1]^+$ (52), 345 $[M+1-H_2O]^+$ (22), 261 $[M+1-C_4H_6O_3]^+$ (74), 245 $[M+1-C_4H_6O_3-O]^+$ (30), 243 $[M+1-C_4H_6O_3-H_2O]^+$ (100), 231 (45), 215 (46), 146 (46), 87 (32); IR $\nu_{max}^{neat}$ superimposable on IR of authentic **3a** [9].

*Solstitiolide* (**2b**) *and episolstitiolide* (**2c**) (mixture **B**) was also a viscous oil, inseparable by CC, HPLC and TLC; IR $\nu_{max}^{neat}$ cm$^{-1}$: 3490 (OH), 1760, 1730 (CO), 1660, 1640, 1290, 1270, 1170, 1140; $^1$H NMR: Table 3; $^{13}$C NMR: Table 4; CIMS (*i*-butane) *m/z* (rel. int.): 401 $[M+1]^+$ (18), 399 $[M+1]^+$ (48), 363 $[M+1-HCl]^+$ (36), 297 $[M+1-C_4H_6O_3]^+$ (67), 281 (37), 279 $[M+1-C_4H_6O_3-O]^+$ (93), 263 (59), 261 $[M+1-C_4H_6O_3-H_2O]^+$ (84), 245 (74), 243 $[M+1-C_4H_6O_3-2H_2O]^+$ (93), 231 (38), 227 (56), 217 (40), 87 (100), 85 (75).

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