

## Desmethylabietospiran, a Naturally Occurring Self-Gelation Agent

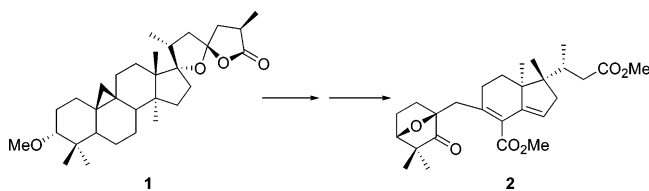
John A. O'Neill,<sup>†</sup> O. Paul Gallagher,<sup>†</sup> Ken J. Devine,<sup>‡</sup> Peter W. Jones,<sup>‡</sup> and Anita R. Maguire<sup>\*,†</sup>

Department of Chemistry, Analytical and Biological Chemistry Research Facility, and Department of Zoology, Ecology and Plant Science, University College Cork, Ireland

Received June 2, 2004

A new self-gelating triterpenoid natural product has been isolated from the bark of the silver fir, *Abies alba*. The structure is desmethylabietospiran (**3**) on the basis of chemical and spectroscopic evidence. Also reported is a more efficient isolation procedure of abietospiran (**1**) from *A. alba*.

The triterpenoid natural product abietospiran (**1**) has been utilized by Corey and Hong in their biomimetic synthesis of the glycinoclepin analogue, 12-desoxyglycinoclepin dimethyl ester (**2**).<sup>1,2</sup> Abietospiran was first isolated from the bark of the silver fir *Abies alba* by Steglich,<sup>3</sup> where the uppermost layer of bark was removed and extracted with hexane in a Soxhlet apparatus. The product (**1**) was obtained by recrystallization from the concentrated extracts. For a recent project, we required abietospiran; when this methodology was applied, it was found that following Soxhlet extraction, silica gel chromatography was necessary to obtain pure **1**. Thus, an alternative means of isolating **1** from *A. alba* was required to achieve a more efficient and economically viable means of acquiring pure **1**.



To obtain sufficient quantity of bark to optimize the isolation procedure, a 10–15 year old *A. alba* tree from Corrin Woods, Fermoy, Co. Cork, Ireland, was felled and the bark removed for extraction. Identification of the harvested tree was authenticated by comparing the needle shape, color, pattern, and smell (needles of *A. alba* have a distinctive citrus fragrance when crushed) to a confirmed sample provided by Fota Arboretum, Cobh, Co. Cork, Ireland. The optimized isolation procedure allowed the isolation of multigram quantities of **1**. Our new procedure negates the need for Soxhlet extraction and chromatography and is amenable to scale-up. The bark is first extracted with dichloromethane at ambient temperature, then the crude extracts are decanted from the bark and concentrated to an oil. The oil is then treated with hot methanol, from which crude abietospiran (**1**) is obtained by crystallization. This is slurried with hexane to remove unwanted impurities. A final recrystallization from ethanol provides abietospiran (**1**) as a pure white solid. The sample of **1** thus obtained was chemically identical to earlier samples obtained by chromatography.

Furthermore, during the course of this study a new natural product, desmethylabietospiran (**3**), was isolated.

The isolation of **3** involved Soxhlet extraction of the crude tree bark with hexane, resulting in an oil, which on trituration with hexane gave a mixture of abietospiran (**1**) and desmethylabietospiran (**3**). The mixture was separated by silica gel chromatography. The hydroxyl compound **3** exhibited interesting physical properties, so that in test tubes containing **3** a gel or membrane formed at the meniscus. In concentrated samples, a gel formed, allowing complete inversion of the tube without any loss of sample. We believe that this phenomenon is worthy of further investigation.<sup>4–6</sup> Examination of the structure of **3** suggests that the gel formation may be due to formation of hydrogen-bonded networks between the secondary alcohol and the spiroactone functionalities located at opposite ends of the molecule. The isolation of **3** is also an interesting result from a biosynthetic viewpoint, as it leads to the possibility that abietospiran (**1**) may be formed in vivo by direct methylation of **3**.

The structure of **3** was assigned by chemical correlation and by  $[\alpha]_D$ , NMR, MS, and IR data. The key chemical correlations, indicated in Scheme 1, involved direct oxidation of **3** with PCC in dichloromethane to give the ketone **4** in a yield of 64%. Oxidative cleavage of the methyl ether functionality of abietospiran (**1**) with ruthenium trichloride and sodium periodate by the method of Sharpless<sup>7</sup> also gave the ketone **4**, albeit in a yield of 29%. The ketone **4** prepared by oxidation of abietospiran (**1**) had an  $[\alpha]^{23}_D +9.45^\circ$  (*c* 1.0 in  $\text{CHCl}_3$ ), compared with a value of  $[\alpha]^{24}_D +9.56^\circ$  (*c* 1.0 in  $\text{CHCl}_3$ ) obtained from the sample of ketone **4** prepared by PCC oxidation of the free alcohol **3**. To confirm that the alcohol **3** is desmethylabietospiran as drawn in Scheme 3, the O-methylation of **3** was performed, which if our structural conclusions were correct, should result in abietospiran (**1**). Methyl triflate (MeTf) has been utilized by Patterson in the presence of 2,6-di-*tert*-butylpyridine (DTBP) to methylate sensitive hindered alcohols.<sup>8</sup> The alcohol **3** was treated with MeTf and DTBP in chloroform at 35–55 °C over 5 h. Purification of the product by silica gel chromatography gave abietospiran (**1**) in 17.5% yield. An optical rotation of  $[\alpha]^{19}_D -15.13^\circ$  (*c* 0.9 in  $\text{CHCl}_3$ ) was obtained for the sample of abietospiran (**1**) prepared by methylation of **3**, compared with a value of  $[\alpha]^{20}_D -16.8^\circ$  (*c* 1.0 in  $\text{CHCl}_3$ ) for the natural product.<sup>3</sup>

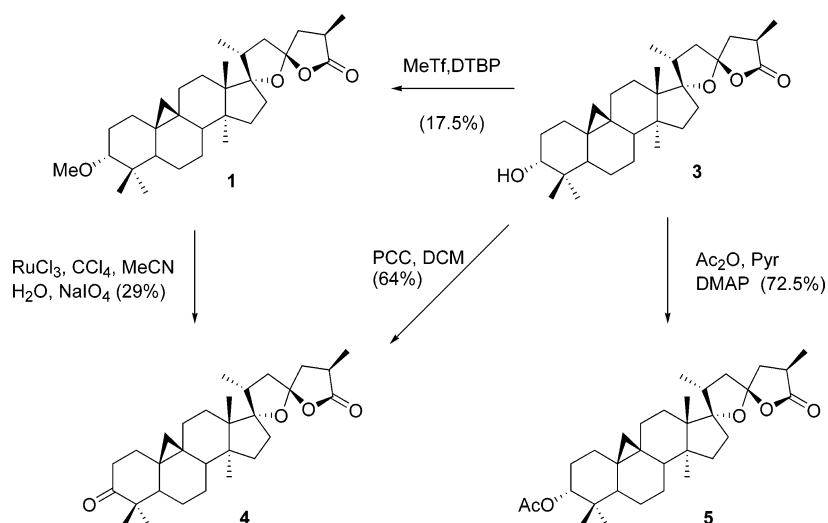
A final chemical confirmation of the structure of **3** was obtained by treatment of alcohol **3** with acetic anhydride and 4-dimethylamino pyridine in pyridine to give the acetate **5** in 72.5% yield. The acetate **5**, with the configuration shown in Scheme 1, has been previously isolated from the bark of *A. marocana* by Sanchez.<sup>9</sup> The <sup>1</sup>H and <sup>13</sup>C NMR data of abietospiran (**1**), the alcohol **3**, the ketone **4**, the acetate reported by Sanchez,<sup>9</sup> and our acetate **5** are

\* To whom correspondence should be addressed. Phone: +353 21 490 2125. Fax: +353 21 427 4097. E-mail: a.maguire@ucc.ie.

<sup>†</sup> Department of Chemistry, Analytical and Biological Chemistry Research Facility.

<sup>‡</sup> Department of Zoology, Ecology and Plant Science.

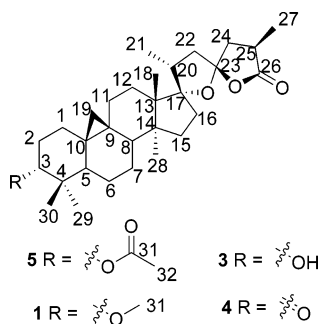
## Scheme 1

**Table 1.**  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz) of Compounds **1**, **3**, **4**, and **5**

| proton        | acetate isolated<br>by Sanchez<br>$\delta$ ppm | acetate <b>5</b><br>$\delta$ ppm    | alcohol <b>3</b><br>$\delta$ ppm    | abietospiran <b>1</b><br>$\delta$ ppm | ketone <b>4</b><br>$\delta$ ppm     |
|---------------|--|-------------------------------------|-------------------------------------|---------------------------------------|-------------------------------------|
| H-19          | 0.36 (1H, d, $J$ 4.1 Hz)                       | 0.38 (1H, d, $J$ 4.3 Hz)            | 0.37 (1H, d, $J$ 4.1 Hz)            | 0.35 (1H, d, $J$ 4.1 Hz)              | 0.60 (1H, d, $J$ 4.3 Hz)            |
| H-19'         | 0.49 (1H, d, $J$ 4.1 Hz)                       | 0.51 (1H, d, $J$ 4.1 Hz)            | 0.50 (1H, d, $J$ 4.1 Hz)            | 0.48 (1H, d, $J$ 4.1 Hz)              | 0.77 (1H, d, $J$ 4.3 Hz)            |
| Me-18         | 0.83 (3H, s)                                   | 0.85 (3H, s)                        | 0.88 (3H, s)                        | 0.87 (3H, s)                          | 1.06 (3H, s)                        |
| Me-28         | 0.91 (3H, s)                                   | 0.93 (3H, s)                        | 0.95 (3H, s)                        | 0.93 (3H, s)                          | 1.10 (3H, s)                        |
| Me-21         | 1.0 (3H, d, $J$ 6.8 Hz)                        | 1.02 (3H, d, $J$ 7.0 Hz)            | 1.02 (3H, d, $J$ 6.8 Hz)            | 1.02 (3H, d, $J$ 8.4 Hz)              | 1.03 (3H, d, $J$ 7.3 Hz)            |
| Me-29         | 1.06 (3H, s)                                   | 1.08 (3H, s)                        | 1.06 (3H, s)                        | 1.04 (3H, s)                          | 1.05 (3H, s)                        |
| Me-30         | 1.16 (3H, s)                                   | 1.18 (3H, s)                        | 1.18 (3H, s)                        | 1.18 (3H, s)                          | 1.21 (3H, s)                        |
| Me-27         | 1.25 (3H, d, $J$ 7.2 Hz)                       | 1.27 (3H, d, $J$ 7.3 Hz)            | 1.26 (3H, d, $J$ 7.0 Hz)            | 1.26 (3H, d, $J$ 7.0 Hz)              | 1.26 (3H, d, $J$ 7.0 Hz)            |
| H-22          | 1.75 (1H, d, $J$ 13.8 Hz)                      | 1.77 (1H, d, $J$ 13.7 Hz)           | 1.76 (1H, d, $J$ 13.5 Hz)           | 1.76 (1H, d, $J$ 13.2 Hz)             | 1.75 (1H, d, $J$ 13.2 Hz)           |
| H-24          | 2.02 (1H, dd $J$ 10.8 &<br>12.6 Hz)            | 2.04 (1H, m)                        | 2.04 (1H, m)                        | 2.02 (1H, m)                          | 2.01 (1H, m)                        |
| Me-32<br>(31) | 2.08 (3H, s)                                   | 2.09 (3H, s)                        |                                     | (3.34) (3H, s)                        |                                     |
| H-20          | 2.2 (1H, dq, $J$ 6.8 &<br>6.8 Hz)              | 2.22 (1H, dq, $J$ 7.0 &<br>7.0 Hz)  | 2.21 (1H, m)                        | 2.21 (1H, dq, $J$ 6.8 &<br>6.8 Hz)    | 2.19 (1H, dq, $J$ 6.6 &<br>6.6 Hz)  |
| H-24'         | 2.49 (1H, dd, $J$ 7.5 &<br>12.6 Hz)            | 2.51 (1H, dd, $J$ 8.1 &<br>12.7 Hz) | 2.50 (1H, dd, $J$ 8.1 &<br>12.7 Hz) | 2.49 (1H, dd, $J$ 8.1 &<br>12.4 Hz)   | 2.46 (1H, dd, $J$ 7.7 &<br>12.1 Hz) |
| H-22'         | 2.71 (1H, dd, $J$ 6.8 &<br>13.8 Hz)            | 2.72 (1H, dd, $J$ 6.3 &<br>13.5 Hz) | 2.72 (1H, dd, $J$ 6.5 &<br>13.5 Hz) | 2.71 (1H, dd, $J$ 6.2 &<br>13.8 Hz)   | 2.68 (1H, dd, $J$ 6.0 &<br>12.5 Hz) |
| H-25          | 2.98 (1H, ddq, $J$ 7.5,<br>10.8, & 7.5 Hz)     | 3.00 (1H, m)                        | 3.02 (1H, m)                        | 2.98 (1H, m)                          | 2.96 (1H, m)                        |
| H-3           | 4.69 (1H, dd, $J$ 2.8 Hz)                      | 4.69 (1H, bs)                       | 3.47 (1H, bs)                       | 2.86 (1H, bs)                         |                                     |

tabulated in Tables 1 and 2 for comparison purposes. The structure of the acetate reported by Sanchez<sup>9</sup> was assigned on the basis of  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^1\text{H}-^1\text{H}$ , and  $^{13}\text{C}-^1\text{H}$  NMR data and MS and IR evidence. The configuration was assigned both directly from the NMR data for the acetate and by correlation of these data with that of other triterpenoid natural products isolated from *A. marocana* by the same group and with related natural products isolated from other sources and confirmed by X-ray crystallography.<sup>9</sup>

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR data reported for the acetate isolated by Sanchez<sup>9</sup> and the data for our acetate **5** are



virtually identical. In particular, the key  $^1\text{H}$  couplings in the spiro-lactone unit for carbons 20–27 are identical, while the key methine proton at C3, observed at 4.69 ppm (t,  $J$  = 2.8 Hz) in the acetate reported by Sanchez, was seen at 4.69 ppm (br s) (270 MHz, JEOL) in our acetate **5**. Comparison of the  $^{13}\text{C}$  NMR for the acetate reported by Sanchez and our acetate **5** shows them to be virtually identical. However, the chemical shift for C14 was not reported by Sanchez.

In addition both the low-resolution EI mass spectrum of the compound reported by Sanchez<sup>9</sup> and our compound **5** gave molecular ions  $[\text{M} + 1]^+$  at 513, corresponding to a molecular formula of  $\text{C}_{32}\text{H}_{49}\text{O}_5$ . The IR spectra reported by Sanchez and our data indicated the presence of an ester [1725 (KBr) and 1720 ( $\text{CH}_2\text{Cl}_2$ ), respectively] and a five-membered lactone [1776 (KBr) and 1768 ( $\text{CH}_2\text{Cl}_2$ ), respectively].<sup>9</sup> However, the acetate reported by Sanchez, recrystallized from diethyl ether, had a melting point of 184–186  $^\circ\text{C}$ , whereas our acetate, recrystallized from hexane, had a melting point of 213–214  $^\circ\text{C}$ ,<sup>10</sup> but perhaps more significantly, Sanchez reported an optical rotation of  $[\alpha]_{\text{D}}^{25} -0.04^\circ$  (c 1.0 in  $\text{CHCl}_3$ ) compared with a value of  $[\alpha]_{\text{D}}^{24} -22.8^\circ$  (c 1.0 in  $\text{CHCl}_3$ ) for our acetate **5**.<sup>9</sup>

**Table 2.**  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz) of Compounds **1**, **3**, **4**, and **5**

| carbon | acetate isolated by Sanchez |   | abietospiran                     |                              |  |
|--------|-----------------------------|---|----------------------------------|------------------------------|--|
|        | $\delta$ ppm                | acetate <b>5</b> <sup>a</sup><br>$\delta$ ppm | alcohol <b>3</b><br>$\delta$ ppm | ( <b>1</b> )<br>$\delta$ ppm | ketone <b>4</b> <sup>b</sup><br>$\delta$ ppm |
| 1      | 25.9                        | 25.9  | 25.9                             | 25.6                         | 25.3   |
| 2      | 25.4                        | 25.4  | 25.4                             | 25.4                         | 45.0   |
| 3      | 79.1                        | 79.1  | 77.0                             | 86.8                         | 216.3  |
| 4      | 38.8                        | 38.8  | 39.6                             | 39.8                         | 50.1   |
| 5      | 42.3                        | 42.2  | 41.1                             | 41.8                         | 48.3   |
| 6      | 21.1                        | 21.0  | 21.1                             | 21.3                         | 21.4   |
| 7      | 25.7                        | 25.6  | 25.6                             | 23.5                         | 25.8   |
| 8      | 49.2                        | 49.1  | 49.0                             | 49.1                         | 48.9   |
| 9      | 20.2                        | 20.2  | 20.1                             | 20.0                         | 21.2   |
| 10     | 26.5                        | 26.5  | 26.6                             | 26.7                         | 26.0   |
| 11     | 26.2                        | 26.2  | 27.5                             | 25.9                         | 26.3   |
| 12     | 28.2                        | 28.2  | 27.5                             | 27.9                         | 33.3   |
| 13     | 49.2                        | 49.1  | 49.1                             | 49.3                         | 48.9   |
| 14     |                             | 49.7  | 49.7                             | 49.7                         | 49.6   |
| 15     | 29.8                        | 29.7  | 28.6                             | 29.7                         | 29.4   |
| 16     | 36.1                        | 36.0  | 36.0                             | 36.1                         | 36.0   |
| 17     | 99.8                        | 99.8  | 99.8                             | 99.8                         | 99.6   |
| 18     | 20.7                        | 20.6  | 20.6                             | 21.5                         | 20.7   |
| 19     | 29.8                        | 29.7  | 29.7                             | 30.0                         | 29.4   |
| 20     | 43.2                        | 43.2  | 43.2                             | 43.2                         | 43.1   |
| 21     | 18.4                        | 18.3  | 18.3                             | 18.3                         | 18.2   |
| 22     | 45.1                        | 45.1  | 45.1                             | 45.1                         | 45.0   |
| 23     | 113.6                       | 113.5   | 113.4                            | 113.4                        | 113.3  |
| 24     | 36.7                        | 36.7  | 36.7                             | 36.8                         | 36.6   |
| 25     | 35.7                        | 35.6  | 35.7                             | 35.6                         | 35.7   |
| 26     | 179.5                       | 179.4   | 179.3                            | 179.2                        | 179.2  |
| 27     | 15.0                        | 15.0  | 14.9                             | 14.9                         | 15.2   |
| 28     | 20.6                        | 20.6  | 20.5                             | 20.7                         | 20.6   |
| 29     | 25.5                        | 25.5  | 25.9                             | 26.0                         | 22.2   |
| 30     | 20.9                        | 20.8  | 21.2                             | 21.1                         | 20.9   |
| 31     | 170.9                       | 170.8   |                                  | 57.3                         |  |
| 32     | 21.5                        | 21.3  |                                  |                              |  |

<sup>a</sup> An additional  $\text{CH}_2$  signal was seen at  $\delta$  21.0. <sup>b</sup> An additional  $\text{CH}_2$  signal was seen at  $\delta$  37.3.

Although a method of isolating abietospiran (**1**) from *A. alba* has been previously reported, this has been the first instance of the isolation and identification of (23*S*,-25*R*)-3 $\alpha$ -hydroxy-17,23-epoxy-9,19-cyclo-9 $\beta$ -lanostan-26,23-olide (**3**) (desmethylabietospiran) in a pure state.

## Experimental Section

**General Experimental Procedures.** Elemental analyses were performed by the Microanalysis Laboratory, University College Cork, using a Perkin-Elmer 240 elemental analyzer. All melting points were determined on a Reichert microscope hot stage melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. IR spectra were run using a Perkin-Elmer 682 spectrophotometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded with a JEOL GSX FT spectrometer (270 and 67.5 MHz, respectively) in  $\text{CDCl}_3$ . Mass spectra were recorded on a Kratos Profile HV-4 double-focusing high-resolution mass spectrometer.

**(23*S*,25*R*)-3 $\alpha$ -Methoxy-17,23-epoxy-9,19-cyclo-9 $\beta$ -lanostan-26,23-olide (**1**) Extraction and Isolation.** The tree bark (1.25 kg) of *A. alba* was extracted with DCM (4  $\times$  3000 mL), and the solvent removed in vacuo. The DCM extracts (17.5 g) were treated with hot MeOH (350 mL), from which the crude compound (4.7 g) was obtained by crystallization. This crude compound (4.7 g) was subsequently slurried with hexane (2  $\times$  35 mL) and finally recrystallized from EtOH (150 mL) to provide pure **1** (3.0 g): mp 212–219  $^\circ\text{C}$  (EtOH), lit.<sup>3</sup> mp 219–221  $^\circ\text{C}$  (EtOAc);  $[\alpha]_{\text{D}}^{20}$  –16.4 $^\circ$  (c 1.0,  $\text{CHCl}_3$ ), lit.<sup>3</sup>  $[\alpha]_{\text{D}}^{20}$  –16.8 $^\circ$  (c 0.68,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  ( $\text{CH}_2\text{Cl}_2$ ) 1768  $\text{cm}^{-1}$  ( $\gamma$ -lactone);  $^1\text{H}$  NMR data, see Table 1;  $^{13}\text{C}$  NMR data, see Table 2; CIMS  $m/z$  (isobutane) 485 [ $\text{M} + 1$ ]<sup>+</sup> (68), 453 (100).

**Synthesis from Alcohol **3**.** A solution of the alcohol **3** (100 mg, 0.213 mmol), 2,6-ditertbutylpyridine (0.5 mL), and methyl

triflate (0.1 mL) in dry  $\text{CHCl}_3$  (10 mL) was stirred at 25  $^\circ\text{C}$  for 16 h under nitrogen. The reaction mixture was then stirred at 35  $^\circ\text{C}$  for 3 h and at 55  $^\circ\text{C}$  for 2 h. Concentrated  $\text{NH}_3$  (5 mL) was added to the reaction, which was stirred at ambient temperature for a further 30 min.  $\text{H}_2\text{O}$  (25 mL) was added and the reaction extracted with EtOAc (2  $\times$  25 mL). The organic extracts were washed with 1 M HCl (4  $\times$  25 mL) and brine (25 mL), dried over  $\text{MgSO}_4$ , and concentrated to an oil in vacuo. The title compound was purified by flash chromatography (silica gel, 20–40% Et<sub>2</sub>O in hexane) as a solid (18 mg, 17.5%):  $[\alpha]_{\text{D}}^{19}$  –15.13 $^\circ$  (c 0.9,  $\text{CHCl}_3$ ), lit.<sup>3</sup>  $[\alpha]_{\text{D}}^{20}$  –16.8 $^\circ$  (c 0.68,  $\text{CHCl}_3$ ).

**(23*S*,25*R*)-3 $\alpha$ -Hydroxy-17,23-epoxy-9,19-cyclo-9 $\beta$ -lanostan-26,23-olide (**3**) (Desmethylabietospiran). Extraction and Isolation.** The tree bark (1.60 kg) of *A. alba* underwent Soxhlet extraction with hexane, after which the solvent was removed in vacuo. The crude oil (23.3 g) was slurried with hexane (2  $\times$  115 mL) to provide a crude solid (3.7 g) as a mixture of the title compound (**3**) and abietospiran (**1**). The crude solid (0.9 g) was purified by flash column chromatography (silica gel, 0–20% Et<sub>2</sub>O in hexane) to provide pure **3** (165 mg). *anal.* C 75.89%, H 10.02%, calcd for  $\text{C}_{30}\text{H}_{46}\text{O}_4$  C 76.55%, H 9.85%; mp 212–214  $^\circ\text{C}$  (MeCN);  $[\alpha]_{\text{D}}^{20}$  +5.45 $^\circ$  (c 1.9,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  ( $\text{CH}_2\text{Cl}_2$ ) 3617 (OH), 1767  $\text{cm}^{-1}$  ( $\gamma$ -lactone);  $^1\text{H}$  NMR data, see Table 1;  $^{13}\text{C}$  NMR data, see Table 2; EIMS  $m/z$  470 [ $\text{M}$ ]<sup>+</sup> (1), 452 (1), 69 (16), 43 (100).

**(23*S*,25*R*)-3-Oxo-17,23-epoxy-9,19-cyclo-9 $\beta$ -lanostan-26,23-olide (**4**). Method A.** Abietospiran (**1**) (484 mg, 1 mmol) was stirred in MeCN (8 mL),  $\text{CCl}_4$  (8 mL), and  $\text{H}_2\text{O}$  (12 mL) at ambient temperature.  $\text{NaIO}_4$  (880 mg, 4.1 mmol) and ruthenium trichloride hydrate (5 mg) were added to the reaction, which was vigorously stirred for 16 h.  $\text{H}_2\text{O}$  (90 mL) was added to the reaction, which was extracted with Et<sub>2</sub>O (2  $\times$  90 mL). The ethereal extracts were washed with saturated aqueous  $\text{NaHCO}_3$  (90 mL) and brine (90 mL), dried over  $\text{MgSO}_4$ , and concentrated to a solid in vacuo. The title compound was purified by flash chromatography (silica gel, 20% Et<sub>2</sub>O in hexane) as a solid (135 mg, 29%). *anal.* C 76.85%, H 9.87%, calcd for  $\text{C}_{30}\text{H}_{44}\text{O}_4$  C 76.88%, H 9.46%; mp 189–195  $^\circ\text{C}$  (hexane);  $[\alpha]_{\text{D}}^{20}$  –9.45 $^\circ$  (c 1.0,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  ( $\text{CH}_2\text{Cl}_2$ ) 1768 ( $\gamma$ -lactone), 1701  $\text{cm}^{-1}$  (ketone);  $^1\text{H}$  NMR data, see Table 1;  $^{13}\text{C}$  NMR data, see Table 2; CIMS  $m/z$  (isobutane) 468 [ $\text{M}$ ]<sup>+</sup> (100), 381 (63).

**Method B.** The alcohol **3** (50 mg, 0.106 mmol) was stirred with pyridinium chlorochromate (100 mg) in dry  $\text{CH}_2\text{Cl}_2$  (5 mL) for 3 h. The title compound was purified by flash chromatography (silica gel, 0–25% Et<sub>2</sub>O in hexane) as a solid (32 mg, 64%):  $[\alpha]_{\text{D}}^{20}$  –9.56 $^\circ$  (c 1.0,  $\text{CHCl}_3$ ).

**(23*S*,25*R*)-3 $\alpha$ -Acetoxy-17,23-epoxy-9,19-cyclo-9 $\beta$ -lanostan-26,23-olide (**5**).** The alcohol **3** (65 mg, 0.138 mmol) was stirred with 4-(dimethylamino)pyridine (1 mg),  $\text{Ac}_2\text{O}$  (0.5 mL), and pyridine (0.5 mL) in dry  $\text{CH}_2\text{Cl}_2$  (2 mL) for 16 h under nitrogen. HCl (1 M, 20 mL) and Et<sub>2</sub>O (30 mL) were carefully added to the reaction. The ethereal layer was separated and the aqueous layer extracted with Et<sub>2</sub>O (15 mL). The combined Et<sub>2</sub>O extracts were washed with saturated aqueous  $\text{NaHCO}_3$  (20 mL) and brine (20 mL), dried over  $\text{MgSO}_4$ , and concentrated in vacuo to an oil. The title compound was purified by flash chromatography (silica gel, 20% Et<sub>2</sub>O in hexane) as a solid (50 mg, 72.5%): mp 213–214  $^\circ\text{C}$  (hexane), lit.<sup>9</sup> mp 184–186  $^\circ\text{C}$ ;  $[\alpha]_{\text{D}}^{20}$  –21.6 $^\circ$  (c 1.0,  $\text{CHCl}_3$ ), lit.<sup>9</sup>  $[\alpha]_{\text{D}}^{25}$  –0.04 (c 1.0  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  ( $\text{CH}_2\text{Cl}_2$ ) 1768 ( $\gamma$ -lactone), 1720  $\text{cm}^{-1}$  (ester);  $^1\text{H}$  NMR data, see Table 1;  $^{13}\text{C}$  NMR data, see Table 2; EIMS  $m/z$  513 [ $\text{M} + 1$ ]<sup>+</sup> (100), 469 (2), 453 (15), 295 (15), 119 (61), 91 (100).

**Acknowledgment.** The authors wish to acknowledge support for this research from Enterprise Ireland and Bio-Research Ireland. In addition a postdoctoral fellowship for P.G. from the Environmental Research Institute/Programme for Research in Third-Level Institutions, which is supported by the HEA and the NDP, is gratefully acknowledged.

## References and Notes

- Corey, E. J.; Hong, B. *J. Am. Chem. Soc.* **1990**, *112*, 8997.
- Corey, E. J.; Hong, B. *J. Am. Chem. Soc.* **1994**, *116*, 3149.

- (3) Steglich, W.; Klar, M.; Zechlin, L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 698.
- (4) Maji, S. K.; Malik, S.; Drew, M. G.; Nandi, A. K.; Banerjee, A. *Tetrahedron Lett.* **2003**, *44*, 4103.
- (5) Clavier, G.; Mistry, M.; Frederic, F.; Pozzo, J. *Tetrahedron Lett.* **1999**, *40*, 9021.
- (6) Stock, H. T.; Turner, N. J.; McCague, R. *J. Chem. Soc., Chem. Commun.* **1995**, 2063.
- (7) Sharpless, K. B.; Carlsen, P. H.; Katsuki, T.; Martin, V. S. *J. Org. Chem.* **1981**, *46*, 3937.
- (8) Paterson, I.; Ward, R. A.; Smith, J. D.; Cumming, J. G.; Yeung, K. *Tetrahedron* **1995**, *51*, 9437.
- (9) Sanchez, J. F.; Barrero, A. F.; Alvarez-Manzaneda, E. J.; Dorado, M.; Haidour, A. *Phytochemistry* **1994**, *35*, 1271.
- (10) Solvent trapped in the crystalline lattice may explain the different melting points observed when crystallised from different solvents.

NP049816U