6. Osaka, Y. and Kenkyushc, K. K. (1983) *Jpn. Kokai Tokkyo Koho JP* **5823**, 612.
7. Kasprzyk, Z., Kochman, K. and Pass, L. (1962) *Bull. Acad. Polon. Ser. Sci. Biol.* **10**, 457.
8. Nishimura, H. and Noma, Y. (1982) *Agric. Biol. Chem.* **46**, 2601.
9. DeMartinez, M. V., deVenditti, F. G., deFenik, I. J. S. and Catalan, C. A. N. (1982) *An. Asoc. Quim. Argentina* **70**, 137.
10. Uzarewicz, I. and Uzarewicz, A. (1976) *Roczniki Chem.* **39**, 1051.
11. De Pascual Teresa, J., Glananes, B., Diaz, F. and Grande, M. (1979) *An. Quim.* **75**, 1001.

Phytochemistry, Vol. 25, No. 1, pp 253–254, 1986.
Printed in Great Britain.

0031-9422/86 $3.00 + 0.00

(−)-3β-ACETOXYDRIMENIN FROM THE LEAVES OF *DRIMYS WINTERI*

JORGE R. SIERRA, JOSÉ T. LÓPEZ and MANUEL J. CORTÉS

Facultad de Química, Pontificia Universidad Católica de Chile, Casilla 6177, Santiago, Chile

(*Received* 20 *May* 1985)

Key Word Index—*Drimys winteri*; Winteraceae; Canelo; leaves; drimane sesquiterpene; (−)-3β-acetoxydrimenin.

Abstract—A new natural product, 3β-acetoxydrimenin was isolated from the petrol extract of the leaves of *Drimys winteri* which also contains the known compounds safrol, drimenol and polygodial. The structure of the new compound was determined by chemical and spectroscopic methods.

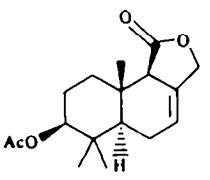
INTRODUCTION

The stem bark of the South American tree *Drimys winteri* Forst has been shown to contain sesquiterpenoids of the drimane type [1, 2]. Further investigation of the leaves afforded cryptomeridiol, cirsimaritin, quercetin, astilbin and quercitrin [3].

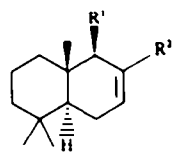
We now report the isolation and structure determination of 3β-acetoxydrimenin (**1**), a new drimane sesquiterpene, from leaves of *D. winteri*, together with the previously known compounds safrol [4], drimenol (**2**) [1] and polygodial (**3**) [5]. To the best of our knowledge, only two drimane sesquiterpenes oxygenated at C-3*, have been found in nature. These are iresin (ent-drimane) from *Iresine celosioides* [6, 7] and uvidin B isolated from *Lactarius uvidis* Fries (Basidiomycetes) [8].

RESULTS AND DISCUSSION

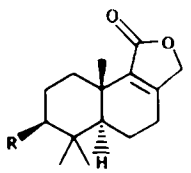
The petrol extract of *D. winteri* leaves afforded safrol [4], drimenol (**2**) [1], polygodial (**3**) [5] and a new drimane sesquiterpene identified as 3β-acetoxydrimenin (**1**) on the basis of the following evidence. The formula $C_{17}H_{24}O_4$ for compound **1** is supported by elementary analysis and mass spectral data. Its IR spectrum shows absorption bands at 1760 and 1725 cm^{-1} confirming the presence of saturated γ-lactone and acetoxyl groups. The ^1H NMR spectrum of **1** shows resonances for three tertiary methyl groups at δ0.94 (6H, *s*, 2 × Me) and 1.00 (3H, *s*, Me), and for one acetate group at δ2.1 (3H, *s*). The



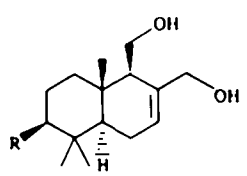
1



2 R¹ = CH₂OH, R² = Me
3 R¹ = R² = CHO



4 R = OAc
5 R = OH



6 R = OH
7 R = H

*We have numbered the C-atoms according to the usual trivial names.

proton geminal to the acetoxyl appears at δ4.5 as a multiplet, superimposed with a signal due to the protons of the lactone ring. A multiplet at δ5.8 is assigned to the vinylic proton at C-7.

Treatment of **1** with methanol–sodium bicarbonate, results in the migration of the double bond from C-7 to C-8 to give **4**. The presence of an α,β-unsaturated γ-lactone in **4**, is indicated by a UV absorption at λ_{max} 216 nm (log ε = 4.02) and a strong IR absorption band at 1725 cm^{-1}. In addition, the ^1H NMR spectrum of **4** shows at δ2.02 (*s*, 3H) the resonance of acetate and contains no signal for a vinylic proton. The migration of the double bond from C-7 to C-8 in compound **4** is a well known isomerization since in basic conditions drimenin is transformed to isodrimenin [2, 9]. By treatment of either **1** or **4** with methanol–potassium hydroxide (2 M), compound **5** is obtained. The IR spectrum of **5** showed hydroxyl (3420 cm^{-1}) and lactone (1725 cm^{-1}) absorptions. In the ^1H NMR spectrum the geminal proton to the secondary hydroxy group appears at δ3.28 as a doublet of doublet with $J_{AX} + J_{BX}$ = 16 Hz. The value of 16 Hz is characteristic of axial–axial and axial–equatorial coupling with the vicinal protons and indicated that H-3 is axial and thus the 3-hydroxyl group is equatorial. Chemical support for the structure of **1** was obtained by lithium aluminium hydride reduction of the natural product (**1**) to give a triol (**6**) identical in all aspects (except optical rotation) with racemic **6** previously obtained by biological oxidation of (±)-7 [10].

The absolute configuration of this sesquiterpenoid (**1**) was not ascertained. However, we suppose that **4** belongs to the normal drimane series, since this absolute configuration has been found in all the sesquiterpenes isolated from *Drimys* species [1, 2].

EXPERIMENTAL

Mps are uncorr. Identities of compounds were established by mmp, IR and ^1H NMR comparison. Petrol is the bp fraction 60–80°. CC was performed on silica gel 100 (Merck 0.063–0.2 mm). IR spectra were recorded using KBr discs. ^1H NMR spectra were recorded at 100 MHz with TMS as int. standard.

Drimys winteri was collected in Santiago, Región Metropolitana (Chile) during March (southern hemisphere, autumm), and a voucher specimen has been deposited in the University herbarium.

Extraction. The shade dried powdered leaves (1 kg) were extracted with petrol for 3 days. Concn gave 100 g.

Chromatography of petrol extract. The extract (100 g) was chromatographed on silica gel. Elution with petrol–EtOAc (19:1) gave safrol (1.9 g) [4]; spectral data identical with those of an authentic sample. Elution with petrol–EtOAc (9:1) yielded drimenol (**2**), needles from hexane (0.7 g) mp 95–97° (lit. [1] mp 97–98°), $[\alpha]_D^{20}$ −16° (C_6H_6; *c* 1.02) and polygodial (**3**), needles from pentane (0.9 g), mp 55–57° (lit. [5] mp 57°); UV λ_{max}^{EtOH} nm (log ε): 226 (4.3).

Naphtho [1,2c] *furan*-1(3H)-*one*-(7S)-*acetoxy*-5,5a,6,7,8,9,9a,9b-*octahydro*-6,6,9a-*trimethyl*-[5aS-(5aα,9aβ,9bα)] (7-β-*acetoxy*-*drimenin*, **1**). Elution with petrol–EtOAc (4:1) gave compound **1**, which crystallized from EtOAc–*n*-hexane (0.22 g) as an amorphous powder, mp 173–174°; $[\alpha]_D^{20}$ −7.0° ($CHCl_3$; *c* 0.9); IR ν_{max} cm^{-1}: 1760 (CO, δ-lactone), 1725 (CO acetate), 1250 (CO ester); ^1H NMR (100 MHz, $CDCl_3$): δ0.94 (6H, *s*, 2 × Me-4), 1.00 (3H, *s*, Me-10), 2.10 (3H, *s*, OAc), 4.64 (3H, *m*, 2 × H-12 and H-3), 5.78 (1H, *m*, H-7). EIMS (70 eV), *m/z* (rel. int.): 292 [M]$^+$ (8) ($C_{17}H_{24}O_4$), 250 [M − CH_2=C=O] (12), 232 [M − AcOH] (37), 217 [M − AcOH − Me] (9), 173 (18), 122 (75), 107 (21), 42 (100); (Found: C, 69.60; H, 8.41. $C_{17}H_{24}O_4$ requires: C, 69.83; H, 8.27%).

Alkaline isomerization of **1**. To a satd soln of $NaHCO_3$ in MeOH (30 ml) was added compound **1** (80 mg) and the mixture was kept at room temp. for 1 hr. Usual work-up gave lactone **4**, which was crystallized from EtOAc–*n*-hexane, mp 171–172°; $[\alpha]_D^{20}$ +81.1° ($CHCl_3$; *c* 1.03); UV λ_{max}^{MeOH} nm (log ε): 216 (4.02); IR ν_{max} cm^{-1}: 1725 (*s*, CO unsatd δ-lactone and CO acetate), 1650 (C=C), 1260 (CO ester); ^1H NMR (100 MHz, $CDCl_3$): δ0.93 (6H, *s*, 2 × Me-4), 1.16 (3H, *s*, Me-10), 2.05 (3H, *s*, OAc), 4.55 (3H, *m*, 2 × H-12 and H-3).

Treatment of **1** *with* KOH–MeOH. To a soln of KOH in MeOH (2 M, 30 ml) was added compound **1** (50 mg) and the mixture was kept at room temp. for 12 hr. Conventional work-up gave compound **5**, which was crystallized from EtOAc–*n*-hexane (40 mg), mp 172–173°; $[\alpha]_D^{20}$ −81.4° ($CDCl_3$; *c* 1.2); UV λ_{max}^{MeOH} nm (log ε): 217 (4.05); IR ν_{max} cm^{-1}: 3430 (OH), 1725 (CO unsaturated γ-lactone), 1660 (C=C), 1250 (CO lactone); ^1H NMR (100 MHz, $CDCl_3$): δ0.82 (3H, *s*, Me-4), 1.03 (3H, *s*, Me-4), 1.11 (3H, *s*, Me-10), 3.28 (1H, *dd*, $J_{AX} + J_{BX}$ = 16 Hz, H-3), 4.57 (2H, *s*, 2 × H-12).

$LiAlH_4$ *reduction of* **1**. The lactone **1** (15 mg) was subjected to $LiAlH_4$ reduction in dry Et_2O. After usual work-up compound **6** was obtained (10 mg), which was crystallized from EtOAc, mp 165–166°; $[\alpha]_D^{20}$ −10.9° (MeOH; *c* 1.1); IR ν_{max} cm^{-1}: 3500–3020 (*s*, OH); ^1H NMR (100 MHz, $CDCl_3$): δ0.76 (3H, *s*, Me-4), 0.85 (3H, *s*, Me-4), 0.97 (3H, *s*, Me-10), 3.6–4.4 (5H, *m*, 2 × H-11, 2 × H-12, H-3), 3.85 (1H, *m*, H-7). The chiral triol **6** was identical with an authentic sample of racemic compound [10] (Co-TLC, IR, ^1H NMR).

Acknowledgements—We wish to express our thanks to Dirección de Investigación, Pontificia Universidad Católica de Chile for financial support (Grant 30/84). The authors are greatly indebted to Dr. Steven V. Ley, Imperial College, London, for a sample and spectra of compound **6**.

REFERENCES

1. Appel, H. H., Brooks, C. J. W. and Overton, K. H. (1959) *J. Chem. Soc.* 3322.
2. Appel, H. H., Connolly, J. D., Overton, K. H. and (in part) Bond, R. P. M. (1960) *J. Chem. Soc.* 4685.
3. Cruz, A., Silva, M. and Sammes, P. G. (1973) *Phytochemistry* **12**, 2549.
4. Devon, T. K. and Scott, A. I. (1975) *Handbook of Naturally Occurring Compounds*, Vol. I. Academic Press, New York.
5. Barnes, C. S. and Loder, J. W. (1962) *Aust. J. Chem.* **15**, 322.
6. Djerassi, C., Sengupta, P., Herran, J. and Walls, I. (1954) *J. Am. Chem. Soc.* **76**, 2966.
7. Djerassi, C. and Burstein, S. (1959) *Tetrahedron* **7**, 37.
8. De Bernardi, M., Mellerio, G., Vidari, G. and Vita-Finzi, P. (1980) *J. Chem. Soc. Perkin Trans.* 1, 221.
9. Asakawa, Y. and Aratani, T. (1976) *Bull. Chem. Soc. Fr.* 1469.
10. Hollinshead, D. M., Howell, S. C., Ley, S. V., Mahon, M., Ratcliffe, N. M. and Worthington, P. A. (1983) *J. Chem. Soc. Perkin Trans* 1, 1579.