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PLAUNOLIDE, A FURANOID DITERPENE FROM *CROTON SUBLYRATUS*

SHUJI TAKAHASHI, MASAAKI KURABAYASHI, EIICHI KITAZAWA*, HIDEYUKI HARUYAMA† and AKIRA OGISO†

Fermentation Research Laboratories, *Chemical Research Laboratories, †Analytical and Metabolic Research Laboratories, Sankyo Co, Ltd, 1-2-58 Hiromachi Shinagawa-ku, Tokyo 140, Japan

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Key Word Index—*Croton sublyratus*, Euphorbiaceae, furanoid diterpene, structural determination, anti-Shay ulcer, clerodane

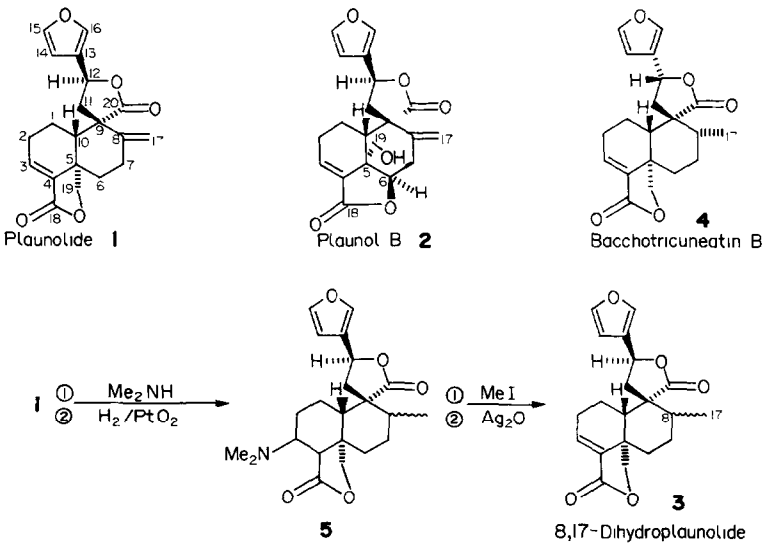
Abstract—The isolation and structural elucidation of plaunolide, a new furanoid diterpene, from *Croton sublyratus* are described

We have recently isolated and characterized diterpene alcohols [1–4] with antipeptic ulcer activity from a crude drug, named plau-noi in Thailand, which is prepared from stems of *Croton sublyratus* Kurz [5]

From the acetone extract of this plant we have isolated another major component named plaunolide (**1**) Compound **1**, $C_{20}H_{20}O_5$ (mass spectral and elemental analysis), contained two γ-lactone ring systems (IR ν cm^{-1} 1775, 1750), a β-monosubstituted furan moiety [IR ν cm^{-1} 3140, 1505, 875, ^{1}H NMR δ 7 64, 7 56, 6 50 (1H × 3, narrow multiplet each), MS *m/z* 95, 94, 81] and an end methylene function [IR νcm^{-1} 1645, 895, ^{1}H NMR δ5 06, 4 82 (1H × 2, narrow doublet each)] The spectral and chemical properties of **1** closely resembled those of plaunol B (**2**) [2, 3] which was isolated previously from the same plant and characterized as a furanoditerpene lactone of the ent-clerodane type On comparison of the ^{1}H NMR spectrum of **1** with that of **2**, it was clear that the hydroxymethyl group at C-5 of **2** was attached to C-18 to form a γ-lactone in the case of **1**, as shown by the absence from **1** of a doublet of doublets due to H-6 (cf **2** δ 4 74, 1H, J = 12, 7 Hz) and a downfield shift of an AB-system attributable to H-19 [**2** δ 3 90, 3 54 (J = 11 Hz), **1** δ 4 22, 4 15 (J = 9 Hz)] All the data thus led to formula **1**

To compare **1** with bacchotricuneatin B isolated from *Baccharis tricuneata* (L f) Pers var *tricuneata* by H Wagner *et al* [6, 7], it was converted to 8,17-dihydroplaunolide (**3**) by the route **1** → **5** → **3** The ^{1}H NMR spectrum of **3**, as well as the other spectra, closely resembled that of bacchotricuneatin B (**4**) except for a chemical shift due to Me-17 [**3** δ 1 05 (d, J = 6 Hz), **4** δ 1 14 (d, J = 6 Hz)] This indicated that 8,17-dihydroplaunolide was a stereoisomer of **4** To confirm this result, X-ray analysis of plaunolide was undertaken [8] The structure of plaunolide, solved by the program MULTAN (the final R-factor 0 069), was found to correspond to formula **1**

Finally, the absolute configuration of plaunolide was



determined to be as shown in formula **1** by comparison of the negative Cotton effect in the CD ($\pi \rightarrow \pi^*$ band) of **3** ($[\theta]_{245}^{MeCN} - 75\,200$) with that of **4** ($[\theta]_{245}^{MeCN} - 17\,600$) [7]

EXPERIMENTAL

All mps were uncorr ^{1}H NMR TMS as an int reference

Extraction and isolation Crushed crude drug (81 5 kg) was extracted (× 3) with Me_2CO under reflux After evaporation of the solvent, the residue was fractionated as in ref [3] to give plaunolide (220 g) after Si gel chromatography [C_6H_6–EtOAc (1 1), R_f 0 37] Mp 169–172°, $[\alpha]_D^{23} - 75\,2°$ (Me_2CO, *c* 1 04), MS (75 eV) *m/z* (rel int) 340 $[M]^+$ (76), 310 (100), 292 (20), 229 (43), 149 (42), 95 (12), 94 (6), 81 (3), IR ν_{max}^{nujol} cm^{-1} 3140, 1775, 1755, 1670, 1645, 1605, 1505, 895, 875, ^{1}H NMR (100 MHz, $CDCl_3$) δ 7 64 (1H, *m*), 7 56 (1H, *m*), 6 64 (1H, *dd*, *J* = 7, 4 Hz), 6 50 (1H, *m*), 5 69 (1H, *dd*, *J* = 7, 8 Hz), 5 06 (1H, *d*, *J* = 2 Hz), 4 82 (1H, *br s*), 4 22, 4 15 (AB system *J* = 9 Hz), 2 02 (1H, *d*, *J* = 8 Hz), 1 58 (1H, *m*) [Found C, 70 10; H, 5 90 $C_{20}H_{20}O_5$ requires C, 70 58, H, 5 92%]

8,17-*Dihydroplaunolide* (**3**) A soln of 2 0 g plaunolide (**1**) and 5 ml dimethylamine in 40 ml THF was kept at room temp overnight After addition of H_2O and EtOAc, the EtOAc layer was extracted with 5% HCl The aq HCl layer was made basic with $NaHCO_3$ and extracted with EtOAc After evaporation of the solvent, the residue was recrystallized from CH_2Cl_2–Et_2O to give 1 8 g of addition product, mp 205–207°, of which 1 35 g was dissolved in 50 ml EtOAc and hydrogenated over 50 mg PtO_2 The usual work-up gave 1 3 g **5**, mp 210–212° A mixture of 2 g **5** and 5 ml MeI in 20 ml MeCN was heated to reflux for 2 hr Usual work-up gave 2 2 g of the desired product, mp 228–230° To a soln of 1 0 g of this product in 10 ml THF and 10 ml H_2O was added Ag_2O (freshly prepared from 2 g $AgNO_3$ and 0 5 g NaOH), and the mixture was heated to 60° for 3 hr Usual work-up gave 0 7 g **3** Mp 189–190°, $[\alpha]_D^{25} - 108\,6°$ ($CHCl_3$, *c* 0 625), MS (75 eV) *m/z* (rel int) 342 $[M]^+$ (0 7), 312 (100), 284 (7 4), 267 (5 1), 239 (6 2), 218 (8 0), 190 (10 5), 173 (8 6), 145 (13 3), 105 (12 6), 95 (26 5), 94 (25 9), 91 (23 7), 81 (14 4), IR ν_{max}^{KBr} cm^{-1} 1755, 1660, 1600, 1510, 1450, 1320, 1195, 1170, 1135, 975, 925, 875, ^{1}H NMR (100 MHz, $CDCl_3$) δ 7 46 (1H, *m*), 7 44 (1H, *m*), 6 70 (1H, *dd*, *J* = 6, 3 Hz), 6 40 (1H, *m*), 5 38 (1H, *t*, *J* = 8 5 Hz), 4 68, 3 85 (2H, ABX, *J* = 9 5, 2 Hz), 2 6–1 2 (12H, *m*), 1 05 (3H, *d*, *J* = 6 Hz) (Found C, 69 87, H, 6 59 $C_{20}H_{22}O_5$ requires C, 70 16, H, 6 48%)

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