

ORGANIC PHOTOCHEMISTRY - PART II¹, PHOTOCHEMICAL SYNTHESIS OF THE NATURALLY
OCCURRING TRITERPENE LACTONE, 3 β -HYDROXY LUPAN-28, 13 β -OLIDE

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Summary : The photochemical synthesis of the title lactone was achieved by irradiation in the presence of Pb(IV) acetate alone or Pb(IV) acetate + calcium carbonate + iodine or mercuric oxide + iodine. Chiroptical measurements (CD) of this and other related lactones provided convincing evidence in support of the lactone ring structure.

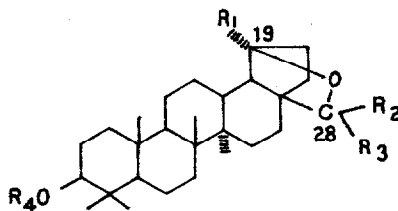
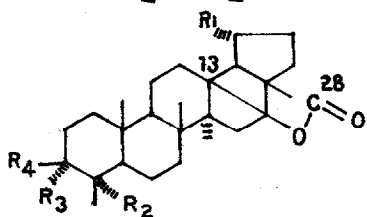
The photochemical synthesis of organic compounds, in many cases, is a convenient technique especially when conventional chemical procedures are difficult to manipulate. Here, we report on the photochemical synthesis of the naturally occurring lactone, 3 β -hydroxy lupan-28, 13 β -olide **1**. The structure of this lactone **1** obtained from *Dilenia indica*², was deduced earlier; but neither synthesis nor stereochemistry has been elaborated. This photochemical synthesis provided an unequivocal proof of its structure and stereochemistry. Also we present here chiroptical measurements (CD) of this and other related lactones of the lupane series.

The key intermediate 3 β -acetoxy dihydrobetulin **4** was prepared from betulinic acid³ **2** as illustrated in the scheme I. **4** in cyclohexane was irradiated with Pb(IV) acetate alone and also separately with Pb(IV) acetate + calcium carbonate + iodine using 250W tungsten lamp for 3 hr, giving same type of products distribution in both cases. Chromatography first eluted **5** (35%) m.p. 158-54°. Its GLC behaviour and spectral characteristics indicated it to be a mixture of 'olefins' resulting from the oxidative removal of -CH₂OH at C-17. **5** was also formed from Pb(IV) acetate oxidation of betulinic acid⁴. The second component eluted was **6** (18%) m.p. 192-4° (α)_D + 17°. A clean photoreaction occurred when **4** was irradiated with HgO + iodine in cyclohexane and **6** was obtained as the sole, isolable product (28%). ¹H NMR revealed tetrasubstituted ether linkage (-C-O-CH₂-) in **6** which must be either C-29, 19 β or C-28, 13 β . **6** on chromium trioxide-AcOH oxidation yielded **7** m.p. 315°. IR band at 1762 cm⁻¹ and absence of ¹H NMR peak around δ 4 established tertiary γ -lactone structure of **7**. **6** and **7** are not identical with Hg(II) acetate oxidation products⁵ dihydro C-28, 19 β -ether **10** and dihydro C-29, 19 β -lactone **11** respectively. Thus, **6** was assigned 3 β -acetoxy-28, 13 β -epoxy lupane and **7** 3 β -acetoxy lupan-28, 13 β -olide which on alkaline hydrolysis afforded **1**, m.p. 321°, (α)_D + 60° [lit.² m.p. 325°(d), (α)_D + 63.4] **7**.

Since in no step of the sequence α -orientation of the C-19 isopropenyl group (isopropyl in dihydro derivative) of betulinic acid **2** was affected, this synthesis proved unequivocally the α -stereochemistry of isopropyl substituent at C-19 in **1**.

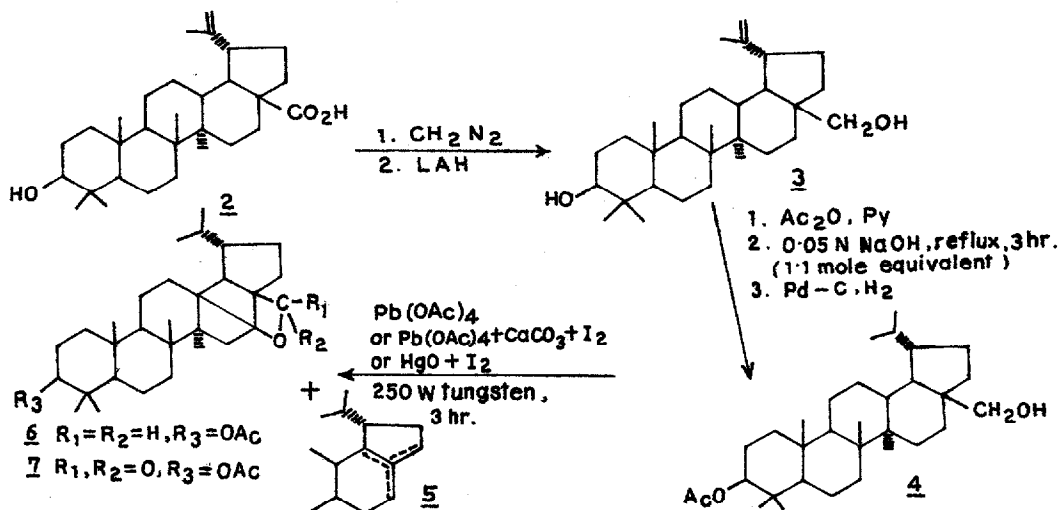
The tertiary γ -lactones of the types **1** and **11** are difficult to distinguish by physical techniques such as IR, ¹H NMR, ¹³C NMR and mass spectral analysis. We obtained CD measurements to distinguish them. Very recently we synthesised⁷ the authentic C-28, 19 β -lactone **12** and C-28, 13 β -lactone

3 and measured their CD spectra. Both the synthetic⁷ lactone 12 and the lactone 11 obtained by Hg(II) acetate oxidation⁵, exhibited negative CE⁷ with maxima at 216 nm ($\Delta\epsilon = -3.6$) and at 217 nm ($\Delta\epsilon = -6.05$) respectively. On the other hand, the synthetic lactone⁷ 8 and the lactone 1 obtained photochemically both showed positive CE having maxima at 219 nm ($\Delta\epsilon = 3.19$) and at 220 nm ($\Delta\epsilon = 1.04$) respectively. We also recorded CD spectrum of epicaltholide 9, another naturally occurring lupane triterpene⁸ having C-28, 13 β -lactone which also exhibited a positive CD band ($\Delta\epsilon = 2.32$ at 217 nm). Thus, CD data provided convincing physical evidence in support of C-28, 13 β -lactone structure for 1 and 9.



- 1 R₁ = isopropyl, R₂ = CH₃, R₃ = H, R₄ = OH
8 R₁ = R₃ = H, R₂ = CH₃, R₄ = OH
9 R₁ = isopropyl, R₂ = R₄ = H, R₃ = OH

- 10 R₁ = isopropyl, R₂ = R₃ = H, R₄ = Ac
11 R₁ = isopropyl, R₂, R₃ = O, R₄ = Ac
12 R₁ = R₄ = H, R₂, R₃ = O



Scheme I : Photochemical synthesis of 3 β -hydroxylupan-28, 13 β -olide.

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