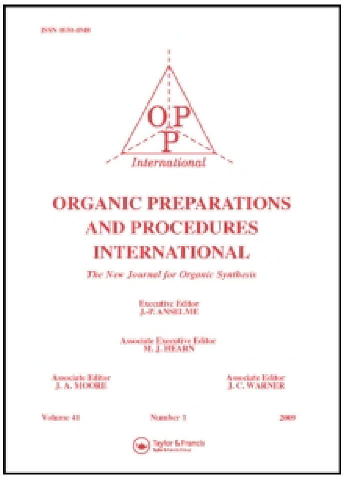

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PARTIAL SYNTHESIS OF GLOCHIDONE

Antonio S. Samson[a]; Robert Stevenson[a]
[a] Department of Chemistry, Brandeis University, Waltham, Massachusetts

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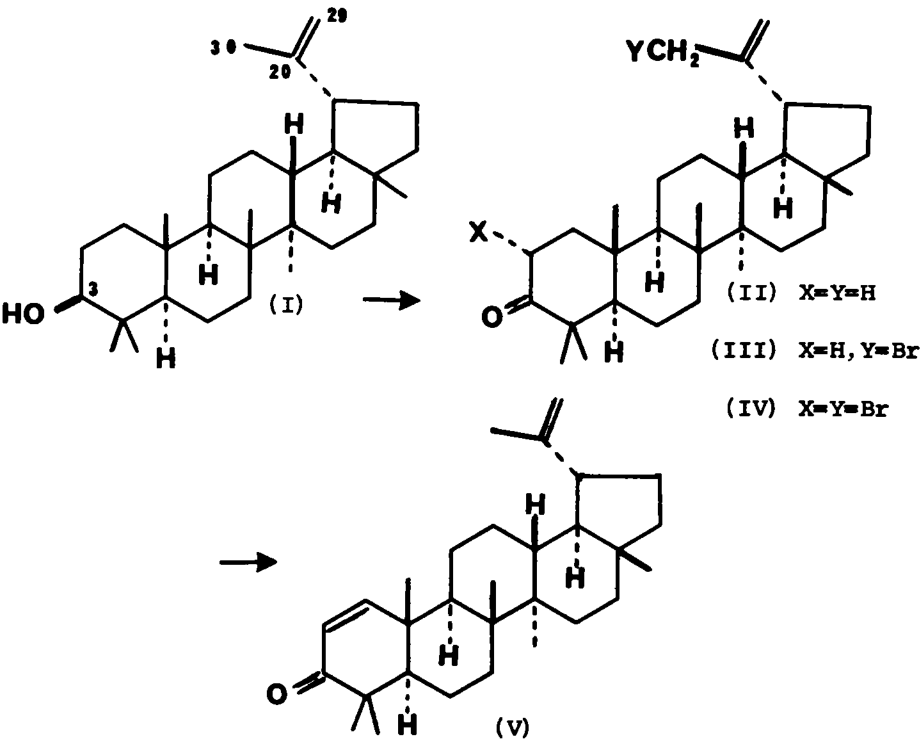
PARTIAL SYNTHESIS OF GLOCHIDONE

Antonio S. Samson and Robert Stevenson

Department of Chemistry
Brandeis University, Waltham, Massachusetts 02154

There have been several recent reports concerning the extractives of the bark, roots, stems and leaves of various species, indigenous to tropical Asia and Australia, of the Glochidion genus (Euphorbiaceae). In 1966, the presence of imidazole alkaloids in one species[1] (probably G. philippicum)



was established, and epilupeol and two new triterpenoids (glochidone and glochidiol) were isolated[2] from *G. hohenackeri*. Since our communication[3] of the conversion of the more widespread triterpenoid lupeol (I) to glochidone (V), Hui and her coworkers have isolated twenty-two compounds from species found in Hong Kong.[4-6] Since nine of these belong to the lupeol triterpenoid class, we report here the experimental details of the synthesis of glochidone from lupeol, which may be of use in structure elucidation by the inter-conversion of these members.

Oxidation of lupeol (I) with Jones reagent[7] gave lup-20(29)-en-3-one (II) in excellent yield. Treatment of this ketone with N-bromosuccinimide (1.2-2.2 mole equivalent) gave both the allylic monobromide, 30-bromolup-20(29)-en-3-one (III) in which the characteristic vinyl methyl group nmr signal of lupeol (τ *ca* 8.3) is replaced by a 2-proton signal at τ 6.00, and the dibromide, 2α,30-dibromolup-20(29)-en-3-one (IV), in which the equatorial (α)-configuration is assigned on the basis of the characteristic shift in the infrared carbonyl absorption.

The dehydrobromination of IV was carried out by treatment with lithium chloride in dimethylformamide.[8] Since examination of the nmr spectrum of the reaction product indicated that partial debromination of the C-30 allyl bromide had also occurred, the desired product, lupa-1,20(29)-dien-

3-one (V) was isolated, without purification at this juncture, after completing the debromination by treatment with zinc dust in ethanol. A mixed mp. and tlc comparison of V with natural glochidone established their identity.[9] The total synthesis of lupeol has recently been announced.[10]

EXPERIMENTAL

Lupenone was obtained as needles, mp.170-170.5° in 90% yield by oxidation of lupeol with Jones reagent[7] for 10 min.

Action of N-Bromosuccinimide on Lupenone. - N-Bromosuccinimide (185 mg: 2.2 molar equivalent) was added to a solution of lupenone (200 mg) in carbon tetrachloride (50 ml) and the mixture heated under reflux. Within 3-5 min., an orange color developed and then disappeared within 30 sec. After 30 min., the mixture was cooled, filtered, the filtrate evaporated and the residue subjected to preparative thin layer chromatography (silica gel PF; developed with and eluted by chloroform).

The faster running constituent (R_f 0.58) was crystallized from chloroform-methanol to give 2α,30-*dibromolup*-20(29)-*en*-3-*one* (IV) as needles (94mg), mp. 232-234°, $[\alpha]_D$ + 18° (c, 1.1 in $CHCl_3$), λ^{KBr} 5.80 μ, τ 6.02s.(allylic $C\underline{H}_2Br$) and 4.8-5.5 (3 protons, overlapping multiplets ($C{=}CH_2$ and CHBrCO).

Anal. Calcd. for $C_{30}H_{46}Br_2O$: C, 61.85; H, 7.96. Found: C, 62.2; H, 7.9).

The slower running constituent (R_f 0.41) was crystallized from chloroform-methanol to give 30-bromolup-20(29)-en-3-one (III) as prisms (115 mg), mp. 181-184°, $[\alpha]_D$+ 19° (c, 0.8 in $CHCl_3$), λ^{KBr} 5.86 μ, τ 6.00s.(allylic CH_2Br), 4.93 and 4.87 (C-29 olefinic protons).

Anal. Calcd. for $C_{30}H_{47}BrO$: C, 71.55; H, 9.41. Found: C, 71.6; H, 9.3.

In larger scale experiments, the dibromolupeone was obtained by direct crystallization from the reaction product mixture.

Lupa-1,20(29)-dien-3-one (Glochidone)(V). - A solution of lithium chloride (4g) in dimethylformamide (50 ml) was added to 2α,30-dibromolup-20(29)-en-3-one (400 mg) in the same solvent (30 ml), the mixture heated under reflux under a nitrogen atmosphere for 4 hr, then worked up in the usual way to give a crude product (351 mg), nmr examination of which showed that there was partial debromination of the allylic halogen in addition to dehydrobromination of the bromoketone function.

Zinc dust (13.5 g) was added to a solution of this product (135 mg) in ethanol (300 ml), the mixture refluxed with vigorous stirring overnight, and worked up in the usual way. Purification by tlc (developed by chloroform) gave a major fraction (R_f 0.32, 117 mg), which crystallized from methanol to give lupa-1,20(29)-dien-3-one as needles mp. 165-166°, $[\alpha]_D$ +67° (c, 1.0 in $CHCl_3$), λ(EtOH) 231 mμ (9900), τ 8.30 s.

(C-30 vinyl methyl), 5.32 and 5.42 m (C-29 olefinic protons), 4.23 d (H-2, J=10 Hz) and 2.92 d (H-1, J=10 Hz). These constants are in excellent agreement with those reported for glochidone and a direct comparison with an authentic specimen confirmed the identity.[9]

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