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A THREE STEP SYNTHESIS OF EXALTOLIDE AND PHORACANTHOLIDE I

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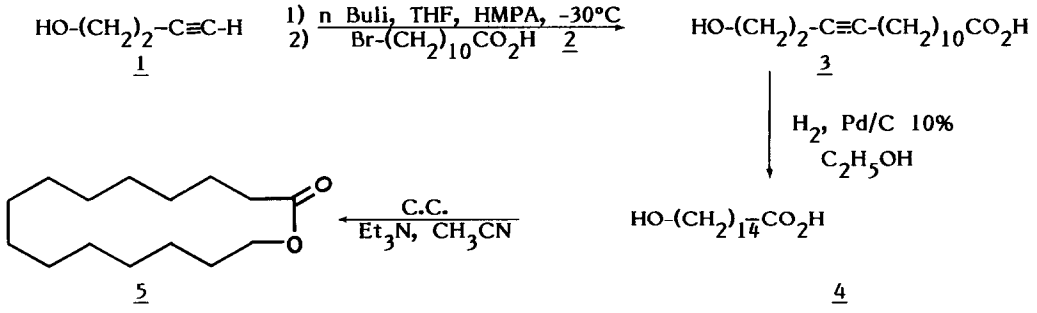
Abstract : The synthesis of phoracantholide I and exaltolide are described in 3 steps and in good yields.

We recently reported a very cheap one step synthesis of ω-hydroxyacetylenic acids. The method involved the chemioselective formation of a C-C bond between ω-acetylenic alcohols and ω-bromoacids (1). The ready availability of the ω-hydroxyacetylenic compounds led us to examine a short synthesis of macrocyclic lactones, and we wish to describe in this letter a new three step synthesis of exaltolide and phoracantholide I. The phoracantholide I (± decan-9-olide) is isolated from the metasternal secretion of the eucalypt longican *phoracantha synonyma* (2). Exaltolide is an important commercially available perfume isolated from angelica root oil (3).

The synthesis of exaltolide is summarised in scheme I.

Scheme I

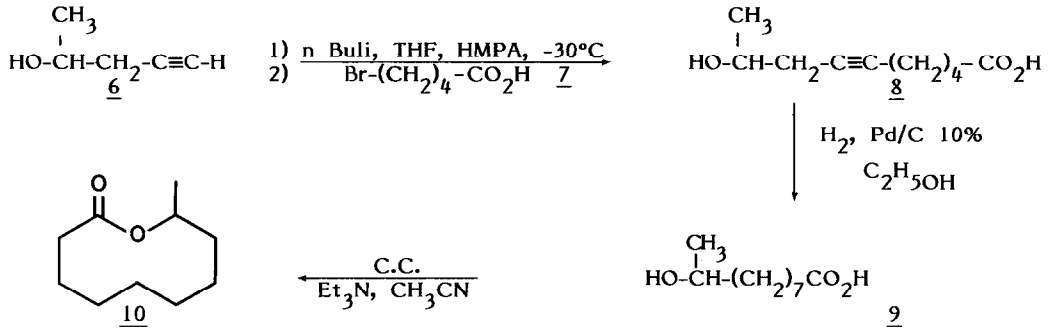


Reaction of 3-butyn-1-ol 1 with n-butyllithium (2 equivalents) and then with 11-bromoundecanoïc acid 2, at -30°C in tetrahydrofuran and hexamethylphosphortriamide (3 equivalents) led to 3 (85%). Hydrogenation of 3 provided 4 (90%) and its cyclisation occured in the presence of cyanuric chloride (C.C.) and triethylamine in acetonitrile at room temperature (4). The exaltolide was thus obtained

with a chemical yield of 50% from 2 (5).

Phoracantholide I was prepared according to scheme II.

Scheme II



Condensation of acetylenic alcohol 6 and 5-bromovaleric acid 7 was obtained with n-butyllithium (2 equivalents) in THF and HMPA (3 equivalents). The ω -hydroxyacetylenic acid 8 (70%) was then hydrogenated to 9 (90%) on Pd/C 10%. The cyclization of 9 in the presence of cyanuric chloride (C.C.) led to (±) phoracantholide I 10 (55%).

These two short synthesis use cheap and commercially available materials and can be compared favourably with the previously described syntheses (6)(7).

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