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AN ALKYLATION WITH THE BIS MANNICH BASE OF ACETONE: A NEW SYNTHESIS OF 3,4-DIHYDROCOUMARINS

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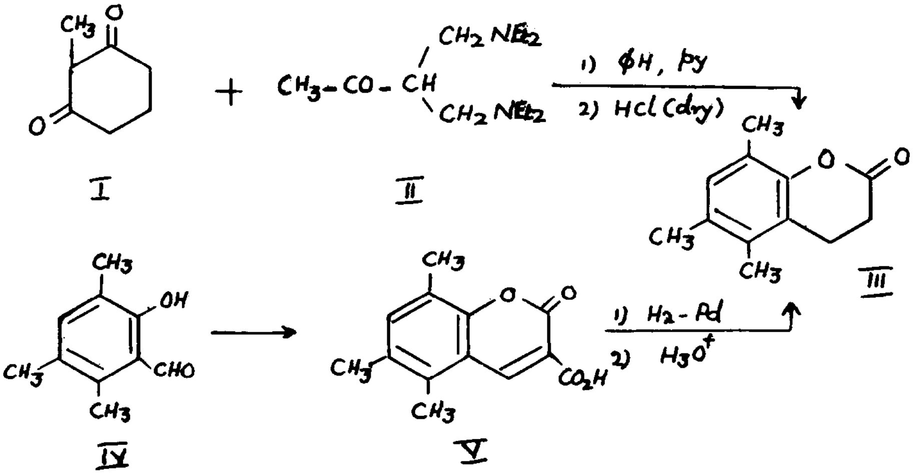
We wish to report an essentially one-step synthesis of 3,4-dihydro coumarins from purely alicyclic precursors.

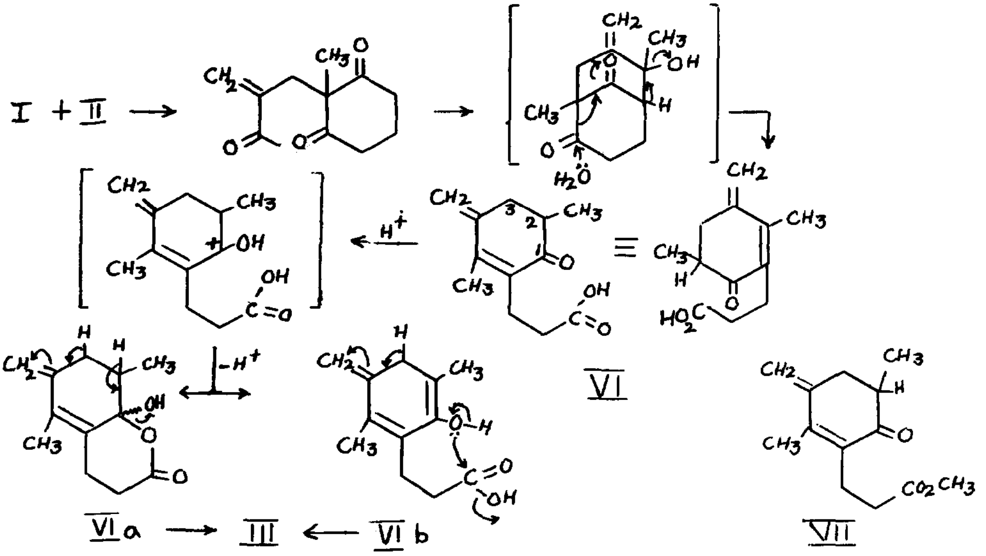
When equimolar amounts of 2-methylcyclohexane-1,3-dione(I) and 1,1-bis-diethylaminomethyl acetone(II) are refluxed together in benzene in the presence of equimolar amount of pyridine and the mixture worked up after treatment with dry hydrogen chloride, a colourless crystalline product(III) m.p.102-103° (EtOH-H_2O) was obtained in 60% yield.* This structure was confirmed by a conventional synthesis from pseudocumenaldehyde(IV).



* The structures of all new compounds were established by elemental analysis and from spectroscopic data.

Catalytic reduction of the acid(V) in HOAc gave (III)[+] identical in all respects (mixed m.p., I.R. and T.L.C.) with the product in the alkylation reaction.

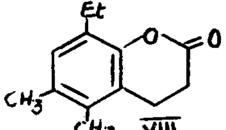
If the reaction mixture obtained in the alkylation of (I) is treated with aqueous hydrochloric acid instead of dry hydrogen chloride, an acid m.p.97-98° is obtained in 50% yield, for which structure (VI) is assigned on the basis of its spectral properties. The acid was readily transformed to (III) by treatment with para toluene sulphonic acid in benzene, or with alcoholic hydrogen chloride. Concentrated hydrochloric acid also effected aromatization slowly. The formation of (III) may be rationalised as follows:



[+] (III) has previously been obtained by one of us[1], although the structure was not rigorously established, as a byproduct in the alkylation of (I) with 1-diethylamino-3-butanone methiodide, which apparently was contaminated with the bis Mannich base methiodide.

The formation of bridged ketols of the type postulated is well documented[2,3]. Attempted aromatization of the free acid in hot pyridine did not give any phenolic acid or coumarin; nor was any phenol formed when the ester (VII) was reacted with ethanolic alkali. Instead, the parent acid was isolated in quantitative yield. These observations seem to indicate that the lactonization may well involve the pseudo acid (VIa) rather than the enolic acid (VIb).

The alkylation of 2-ethyl-1,3-cyclohexane dione with the bis Mannich base of acetone furnished similarly the dihydrocoumarin (VIII), m.p. 76-77°.



VIII

Interestingly, when the reaction was extended to 2-methyl cyclopentane-1,3-dione, instead of any coumarin derivative, a bicyclic ketone has been formed. We are currently investigating its structure.

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