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A NEW SYNTHESIS OF 4-CHROMANONES

Jaime Primo, Rosa Tormo
Departamento de Química, E.T.S.I.I., Universidad Politécnica de Valencia
and Miguel A. Miranda*
Departamento de Química Orgánica, Facultad de Farmacia, Universidad de Valencia, Spain

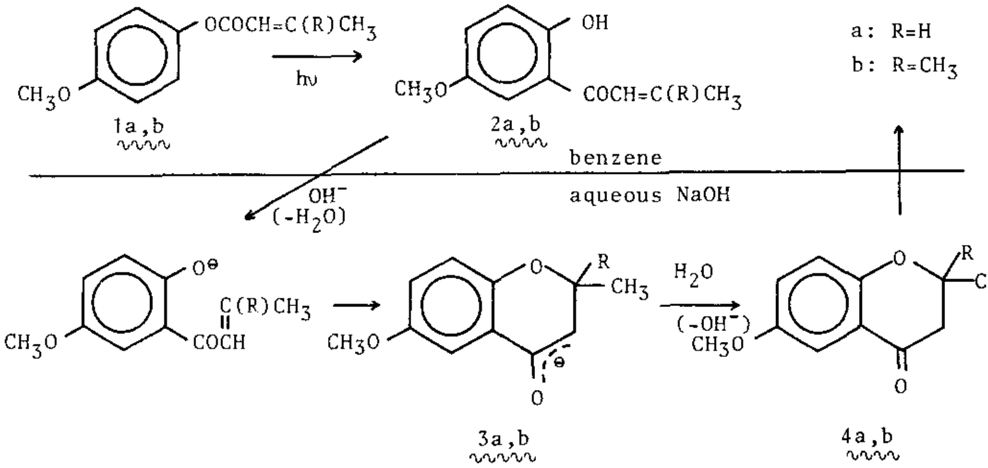
Abstract - Aryl esters of α,β-unsaturated carboxylic acids undergo photorearrangement, followed by basic cyclization, to give 4-chromanones. Reduction/dehydration of these compounds affords 2*H*-chromenes in excellent overall yields.

The discovery that precocenes are potent juvenile hormone inhibitors[1,2] has led to a renewed interest in the synthesis of the 2*H*-chromene unit. Among the most general approaches to this system are the treatment of coumarins with Grignard reagents, the rearrangement of aryl propargyl ethers, the cyclization of *o*-allylphenols and the condensation of phenols with α,β-unsaturated carbonyl compounds.[3,4] However, the development of economical and specific insecticides of this type depends on the availability of even more efficient and selective synthetic methods. We hereby report a new and elegant procedure which provides a direct route to 4-chromanones. As these compounds can be reduced to the corresponding alcohols, which in turn are easily dehydrated,[5,6] the procedure here described constitutes a useful alternative for the preparation of 2*H*-chromenes.

As a continuation of previous work directed to the photochemical synthesis of oxygen heterocycles,[7-10] we planned to check the prospects of a synthetic scheme based on the photo-Fries rearrangement[11,12] of substituted aryl acrylates. In a first stage, 1 g of the model ester **1a** (or **1b**) was irradiated in benzene (300 ml) with a medium pressure mercury lamp and a quartz immersion well. After 10 h, an equilibrium was reached in which only 25 % of the starting material (50 % in the case of **1b**) was present in the reaction mixture. The main products were **2a** (710 mg) or **2b** (460 mg), and the rest was unidentified polymer. Cyclization to **4** took place quantitatively by treatment with 10 % NaOH in a separate step.

Although the reaction was clean and easy to perform and the required conditions were mild as compared to the acid-catalyzed condensation of phenols with α,β-unsaturated acids,[13,14] the overall yields were only moderate, especially in the case of the dimethyl derivative 4b. However, it is noteworthy that the dark reaction of *p*-methoxyphenol with β,β-dimethylacrylic acid in the presence of polyphosphoric acid gives only a 18 % of 4b, apparently due to the lack of an activating substituent at the C-3 position of the phenolic nucleus.[5]

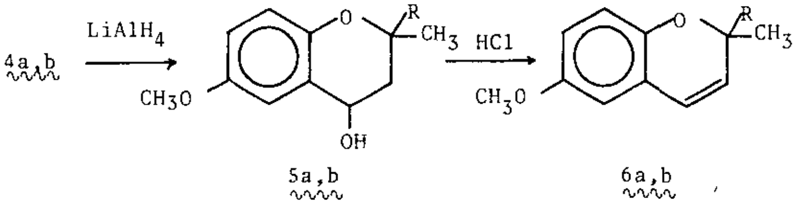
The fact that photochemical rearrangement of 1a,b proceeds only to a limited extent can be probably attributed to the filtering action of *o*-hydroxyketones 2a,b. This would be in accord with the intense UV-absorption of these products and their ability to dissipate the absorbed energy by an intramolecular proton transfer mechanism.[15,16] In order to circumvent this limitation we have modified the initial conditions, carrying out the irradiations in a two-phase system benzene/10 % aqueous NaOH. Operating in this way, chromanones were directly obtained in excellent yields (4a: 91 %, 4b: 82 %).



A plausible explanation for this favourable change could be the following: removal of the photo-Fries products 2a,b from the organic phase is efficiently accomplished by extraction with an alkaline solution, because of the acidity of phenolic hydroxyl groups. Subsequent base-promoted cyclization occurs in the aqueous phase, giving rise to enolates 3a,b. After taking a proton from water, the resulting chromanones 4a,b return finally to the organic phase.

As all possible impurities (p-methoxyphenol, carboxylic acids, etc.) tend to be retained in the alkaline solution, simple evaporation of the organic solvent gives the desired products in pure state.

Reduction of 4a,b with excess lithium aluminium hydride resulted in the formation of chromanols 5a,b and final dehydration with HCl afforded chromenes 6a,b in 90 % yield from 4.



In summary, the alternative now described is an efficient direct route of wide applicability to 2H-chromenes. It requires simple starting materials and easy manipulations. Further synthetic applications are currently being investigated.

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