Molecular Iodine - An Efficient Oxidative Reagent for Aromatization of Trifluoromethyl Substituted Chromenones

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INTRODUCTION

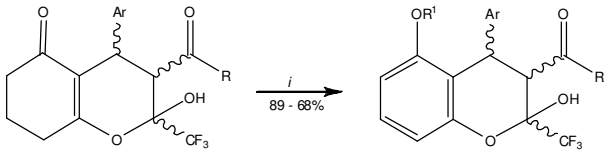
Functionalized chromenes and benzopyranes are important compounds which, due to their biological activity, find wide application in medicinal chemistry. They display not only spasmolytic, diuretic, clotting, antiviral, anti-tumoral and anti-anaphylactic activity, but can also be used as pigments, photo-active materials and biodegradable agrochemicals.[1,2]

The use of molecular iodine as an oxidant to promote aromatization of cyclohexanone derivatives was first reported in 1980 by Tamura and Yoshimoto[3]. In recent years, molecular iodine has received considerable attention as an inexpensive, non-toxic, readily available oxidant to promote aromatization of cyclohexanone derivatives and their heterocyclic analogues.[4,5,6] In this context, herein we describe the synthesis of 5-alkoxy-3,4-dihydro-2*H*-chromenes, using as starting material the trifluoromethylated chromenones recently reported by our research group.[7]

RESULTS AND DISCUSSION

The reactions so far investigated can be seen in Scheme 1. Initially, the reactions of compounds **1** and MeOH/I_2 under reflux were carried out for 16-24 hours, which led to formation of compounds **2** in 65-89 % yields. Subsequently, aromatization reactions of the chromenones were performed using different alcohols (ethanol, *n*-propanol and benzilic alcohol), where **Ar**=Ph and **R**=Me (Scheme1). Only reactions using ethanol and *n*-propanol led to derivatives **2**; for the other alcohols the starting material was recovered.

The chromenes **2** were purified by column chromatography using hexane/ethyl acetate (4:1) as eluent and characterized by NMR ^{1}H, and ^{13}C and GC/MS spectrometry.



i: I_2 (2 equiv.), R^1OH, 70ºC, 16-24 h

Ar: Ph, 4-NO_2Ph, 4-MeOPh

R:Me, Ph, 2-Furyl

R^1: CH_3, C_2H_5, *n*-C_3H_7

(11 examples)

Scheme 1: Synthesis of 5-alkoxy-3,4-dihydro-2*H*-chromenes (**2**)

CONCLUSION

The methodology described, I_2/R^1OH, was efficient and versatile for obtaining of 5-alkoxy-3,4-dihydro-2*H*-chromenes **2,** which contain a benzo[b]pyran, which contain an alkoxy substituent at C-5 derived from the employed alcohol.

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