



Stereoselective hydrogenation of 3-acyl-substituted 2-(trifluoromethyl)-2H-chromen-5-one and chromane scaffolds in NaBH₄/ethanol medium

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INTRODUCTION

Octahydrochromens are compounds that contain a non-aromatic cyclic ether nucleus of tetrahydropyran, which are part of a wide array of natural compounds, as well as synthetic flavors substances. For this reason, there is a clear growth in the employing of some of them as flavor and perfume compounds in certain odorants.¹

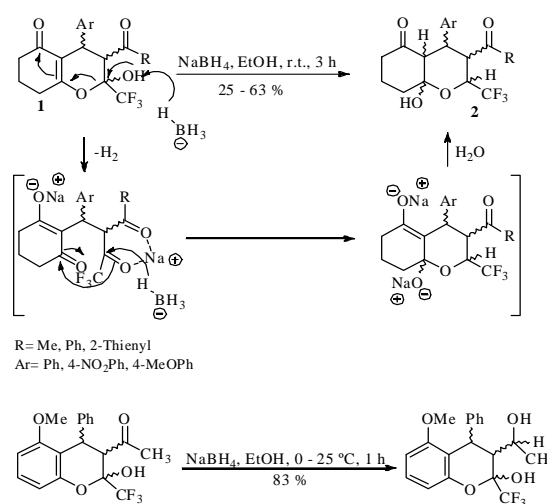
On the other hand, the reducing agent sodium borohydride is commonly used for reduction of unsaturated carbonyl compounds, is becoming a standard method in both academic and industrial laboratories.²

In this context, we describe a synthesis of a new series of substituted octahydrochromenone derivatives (**2**) from the 2-trifluoromethyl-2H-chromenones (**1**) and one example of 3,4-dihydro-2H-chromane (**4**) from the respective 2-(trifluoromethyl)chromane (**3**), employing sodium borohydride/ethanol as an efficient, straightforward and selective reductive reaction medium for these types of heterocyclic compounds.

RESULTS AND DISCUSSION

Initially we investigated the reactions of 2H-chromenones **1** and sodium borohydride (NaBH₄) as the mild reduction agent in different molar ratios (1:1, 1:2, 1:3 and 1:1.2) with different reaction times (0.5 - 3 hours). The best condition was obtained with the 1:1.2 molar ratio (**1**:NaBH₄) for 3 hours at room temperature, employing ethanol as the reaction solvent (Scheme 1).³

In a subsequent step, we also evaluated the behavior of the precursor 5-methoxy-3,4-dihydro-2H-chromane (**3**) in the presence of NaBH₄. The optimal reaction condition was done in ethanol using 1.2 mmol of NaBH₄ at 0 - 25 °C for 1 hour. In this specific example, we isolated only 3-(1-hydroxyethyl)-2-hydroxy-5-methoxy-4-phenyl-2-(trifluoromethyl)-3,4-dihydro-2H-chromane (**4**) as the product with yield 83% (Scheme 1).⁴



Scheme 1.

CONCLUSION

In summary, we applied the well-known method of hydrogenation using NaBH₄/ethanol at room temperature as a mild and straightforward procedure to obtain high regioselectivity and regular to good yields for the unexpected synthesis of new trifluoromethyl-substituted 8a-hydroxy-octahydrochromenones (9 examples) and the 3-(hydroxyethyl)-3,4-dihydro-2H-chromane.

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CNPq-CAPES

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