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Molecular iodine catalyst promoted synthesis of chromans and 4-aryl-3,4-dihydrobenzopyran-2-ones via [3+3] cyclocoupling

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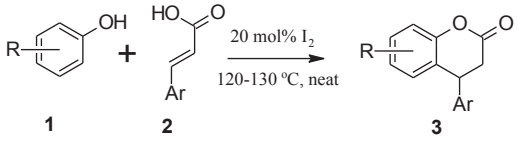
ABSTRACT

Molecular iodine as an inexpensive catalyst is described in the construction of 2-substituted or 2,2-disubstituted chromans and 4-aryl-3,4-dihydrobenzopyran-2-ones via [3+3] cyclocoupling. For the synthesis of chromans, phenols and allylic alcohols were refluxed in chloroform in presence of 20 mol % I_2 while [3+3] cyclocoupling of phenols and cinnamic acids proceeded to give 4-aryl-3,4-dihydrobenzopyran-2-ones using 30 mol % I_2. Later reaction occurs via a tandem hydroarylation–esterification process at 120–130 °C under solvent free conditions. Chromans were obtained in 20–92% yields and substituted 4-aryl-3,4-dihydrobenzopyran-2-ones were obtained in 5–85% yields.

1. Introduction

Molecular iodine is a mild Lewis acid used in plethora of functional group transformations in organic synthesis either as a catalyst or in stoichiometric amount and many reviews have documented its applications.[1] A large number of heterocycles, such as benzofurans, furans, benzothiophenes, thiophenes, benzopyrans, benzoselenophenes, selenophenes, α-pyrones, isocoumarins, isoxazoles, chromones, β-lactams, 2,3-dihydropyrroles, pyrroles, furopyridines, furanones and isochromenes have been prepared by iodine-mediated domino or one-pot multicomponent reactions. Iodine has gained considerable attention as it is readily available, non-toxic, cheap, easy to handle and, hence has become a preferred alternative for toxic and expensive acid catalysts. Also it has high tolerance to air as well as moisture and can be easily removed from reaction systems by washing with reducing agents.

Continuing our interest[2] in catalytic usage of iodine for the synthesis of heterocycles, we in a preliminary communication reported the synthesis of 4-aryl-3,4-dihydrobenzopyran-2-ones via the [3+3] cyclocoupling of phenols with cinnamic acids (Scheme 1).[2b] Herein we disclose full account of our work in exploring iodine as catalyst for the synthesis of chromans and 4-aryl-3,4-dihydrobenzopyran-2-ones. 3,4-Dihydrobenzopyran-2-ones or dihydrocoumarins are well known for fragrance in cosmetics,[3] food flavouring[4] and perfumery industries.[5] 4-Aryl-3,4-dihydro coumarins are naturally occurring compounds[6] exhibiting some interesting biological activities, such as aldose reductase inhibition,[7] antiherpetic,[8] protein kinases[9] and are important synthetic intermediates for pharmaceutical compounds. Many methods are reported for the synthesis of dihydrocoumarins.[10]



Scheme 1. Reaction of phenol with cinnamic acid.

Dihydrobenzopyran (chroman) ring system constitutes the basic unit in number of naturally occurring biologically active scaffolds.[11] It prevalently appears in important bioactive compounds, such as vitamin E or α-tocopherol,[12] flavonoids,[13] etc. Many chroman derivatives are used as antioxidants for fats and oils[14] and some exhibit weak oestrogenic activity.[15] Owing to this property they have attracted the attention of several chemists in recent years and are important drug targets. Most of the reported routes couple phenols and dienes by homogenous or heterogenous acids as catalyst,[16]

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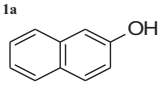
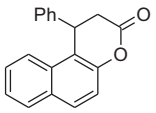
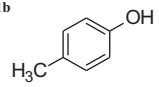
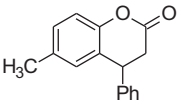
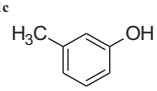
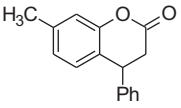
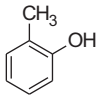
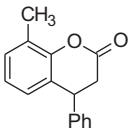
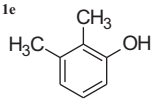
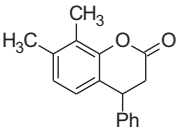
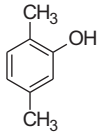
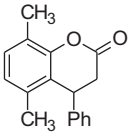
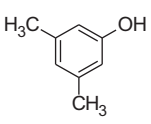
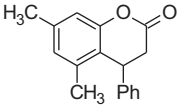
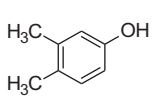
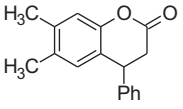
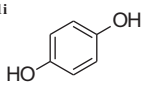
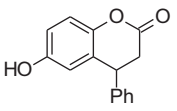
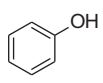
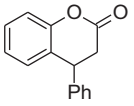
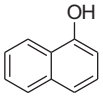
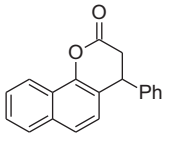
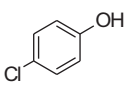
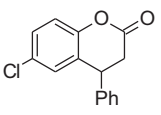
Table 1
Various 4-aryl-3,4-dihydrobenzopyran-2-one derivatives **3a**–**l**, **p**–**z** and substituted phenyl cinnamates **3m**–**o** produced under optimised reaction conditions

Entry	Substituted phenol	Product	Time (h)	Yield (%)[a]
1	**1a** 	**3a** 	1	80
2	**1b** 	**3b** 	1	83
3	**1c** 	**3c** 	1.5	78
4	**1d** 	**3d** 	3	60
5	**1e** 	**3e** 	4	83
6	**1f** 	**3f** 	5	65
7	**1g** 	**3g** 	2	85
8	**1h** 	**3h** 	2	85
9	**1i** 	**3i** 	2	77
10	**1j** 	**3j** 	4	60
11	**1k** 	**3k** 	4	65
12	**1l** 	**3l** 	3	70